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A REFERENCE HANDBOOK

OF

THE MEDICAL SCIENCES

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SCIENTIFIC AND PRACTICAL MEDICINE

AND

ALLIED SCIENCE

BY VARIOUS WRITERS

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Baden-Baden and the Black Forest, Germany.—The region of the Black Forest (Schwarzwald) lying to the east of the Rhine, between Karlsruhe and Basel (Switzerland), is a thickly wooded mountain range of great beauty and picturesqueness, containing many climatic and mineral-water health resorts. The most of these resorts have only a summer season extending from about the middle of May to the end of September; but the open-air cures for pulmonary tuberculosis remain open the whole year, and the winter season is just as efficacious, if not more so, in the treatment of this disease as are the milder seasons of the year. The climate in general is that of Central Europe, with the addition of the peculiar influence of the mountains and the thick fir forests. The elevations of the climatic resorts are from one to two thousand feet. In this country comparable resorts are such places as Rutland, Mass., Saranac in the Adirondacks, and Liberty, N. Y.

Baden-Baden (650 feet) lies at the entrance of the Black Forest from the north, six miles from the Rhine, and is beautifully situated; it is surrounded by hills thickly wooded with the dark fir. It is one of the most popular spas of Europe, and, besides its permanent population of 15,000, it is visited in the summer by about 60,000 people. Moreover, the environs of Baden are most charming, and one can either begin or end a tour of the Black Forest at this point.

The average temperature of the year is 48.3° F., and for the summer as follows: May, 53.9° F.; June, 60.2° F.; July, 62.9° F.; August, 62.2° F.; September, 56.6° F. For the autumn, 47.6° F.; winter, 34.3° F. The yearly rainfall is quite large. The surrounding hills afford shelter from the cold winds in winter, but in midsummer they prevent the cool breezes from mitigating the heat which, for some persons, is too great for comfort.

The waters contain sixteen grains of common salt to the pint, at a temperature of 110° to 154° F. They are used for drinking, but chiefly for bathing, and in various forms of douches. The maladies for which such waters are recommended are rheumatism, gout, lithemia, gastric catarrh, catarrh of the bladder, scrofula, chronic metal poisoning, obesity, and chronic catarrhal affections of the respiratory tract. The effect of the waters when drunk is diaphoretic, diuretic, and laxative. The bath establishments are extensive and well appointed, some of them luxuriously so, and include hot-air, vapor, pine, electric, and mud baths, and swimming pools. There is also an inhalation establishment, and a section for Swedish massage and mechanical gymnastics. There is an elaborate and extensive *Conversations-Haus* with pleasant grounds, and near at hand is a *Drink-halle*, most frequented in the early morning, when the waters are drunk to the accompaniment of music, the usual custom in European spas. There are also several private sanatoria under competent direction. The sanitary condition of the city is satisfactory, and the water supply for domestic purposes comes from mountain wells. The accommodations are abundant, excellent, and of varying price. The baths are open all the year, although they are most frequented during the season (May to October). There are also milk, herb, and grape cures. The situation of Baden with its hills affords opportunity for the "Terrain-Cur." One can also make an "after-cure" here after a course of more active mineral waters.

East of Baden-Baden, in the northeastern part of the Black Forest, is *Wildbad* (1,410 feet), a much-frequented spa, containing indifferent thermal waters, of a temperature of 91.3° to 104.5° F., used very largely for bathing, although they are also used for drinking and gargling. The town, of about 3,000 inhabitants, lies in the narrow wild valley of the Enz, surrounded by hills covered with pines, and possesses an agreeable climate and excellent drinking-water. The mean yearly temperature is 46.5° F., and the mean monthly temperatures for the season are: May, 53.7° F.; June, 60.8° F.; July, 63.1° F.; August, 62.6° F.; September, 55.9° F. The waters are beneficial for the class of cases for which simple hot baths are appropriate, such as chronic rheumatism, gout, chronic joint pains, metal poisoning, scrofula, functional nervous affections, catarrah of the respiratory organs, nervous dyspepsia, convalescence from acute and chronic diseases, certain gynecological affections, and chronic skin eruptions. The bracing mountain air found here also enhances the value of a visit to this resort. The application of the waters is chiefly in bathing, and they are conducted from the wells in a continual stream at their natural temperature. There are also electric, steam, and hot-air baths; massage and gymnastics. There are several bath establishments, the property of the Government, two excellent ones, the Great Bathhouse and the König Karls Bad, and others for the poor or those of slender means. There are a variety of outdoor amusements, such as fishing, shooting, and tennis; and, as in almost all these resorts so largely visited by English and Americans, an English church.

Not far from Wildbad is *Schomberg* (2,130 feet), where are situated a number of sanatoria for pulmonary tuberculosis.

St. Blasien (2,530 feet), in the southeastern part of the Black Forest, has an excellent climate and situation, affording mountain and forest air, and is resorted to, both in summer and in winter. There are pleasant walks among the forests in the neighborhood, and the paths are arranged for the "Terrain-Cur." There is a well-known sanatorium here, open the whole year for the open-air treatment of pulmonary tuberculosis.

At *Nordrach* (1,470 feet), near the center of the Black Forest, existed for many years Dr. Walther's celebrated "Nordarch-Colonie," in a protected position, looking toward the south. The success of Dr. Walther in the treatment of pulmonary tuberculosis has given this place and name a world-wide fame.

The climate at all these open-air resorts in the Black Forest is practically the same: the air is fresh and pure, fairly dry and equable, and although cold in winter (mean winter temperature, 29.6° F.) it is sunny and there is protection from the wind. The mountain influence is also apparent, and the thickly wooded character of the country is not without value.

Badenweiler (1,450 feet), in the lower part of the Black Forest, is a popular summer resort and spa, and possesses great beauty of situation and an excellent climate, pure air with a moderate humidity of seventy per cent., and an equable, mild temperature. The mean average monthly temperatures are: May, 53.8° F.; June, 61.5° F.; July, 64.6° F.; August, 62.8° F.; September, 57.4° F. The yearly rainfall is about forty inches. Badenweiler is used much more for a climatic health resort than for its waters, which are indifferent thermal (of 84° F.). They are used in drinking, in gargling, and in baths, and for various maladies—gout, rheumatism, neurasthenia, chronic neuralgia, diseases of the skin, catarrh of the respiratory passages, dyspepsia, dysmenorrhea, etc. There are two public bathing pools, the "beautiful marble bath," an open swimming pool, and bath-rooms in a number of hotels. The baths are sometimes artificially heated, and common salt is added to render them more stimulating. The milk and whey cures can also be taken here. The sanitary conditions of the town and the water supply are good. There is also a steam disinfecting apparatus. The accommodations are good in hotels and pensions. In the vicinity of Badenweiler are various resorts of different elevations which offer favorable climatic conditions.

Rippoldsau (1,856 feet) is situated in about the center of the Black Forest near the Kniebis Mountains, in a thickly wooded valley, with typical forest scenery, rocky precipices, cascades, and the ever-present fir trees. The waters are gaseous chalybeate, containing bicarbonate of iron, sulphate of sodium, carbonate of calcium, and free carbonic acid gas. The waters are taken internally in anemia, chlorosis, debility, dyspepsia, catarrhal conditions of the stomach and bowels, etc. Iron baths are also used from two springs containing a small amount of iron and rich in carbonic acid gas. Mud baths are used extensively here, and are said to be effective in chronic rheumatic swellings, various sexual disturbances such as amenorrhea, spermatorrhea, and impotence. There are also pine-needle, electric, and sand baths, with massage and gymnastics. The baths are heated by Schwarz's method, which consists of the introduction of steam into the double bottoms of the separate baths. There are two well-appointed bathhouses containng twenty-five bath-rooms. The yearly average is about thirty-five hundred baths. The water from some of the springs, viz., Josef's, Leopold's, and Wenzel's, are bottled and largely exported, as is also the salt (Rippoldsau salts). The accommodations are good. The rural simplicity of the place remains, many of the old-time costumes being still worn by the natives.

There are numerous other small spas and climatic resorts in the Black Forest, all attractively situated and affording opportunities for hydrotherapeutic treatment or open-air life in a fresh invigorating atmosphere. Indeed, a walking, bicycle, or automobile tour through this most picturesque region may well be considered a cure in itself for tired nerves and the mentally overworked; and the writer, from personal experience, can bear witness to the charm and restfulness of such an excursion: the air is so fresh and invigorating, the food so good, the country scenery so attractive, and the singing of the skylarks so sweet and seductive.

EDWARD O. OTIS.

Bado, Sebastian.—(The name is also spelled Baldus.) A Genoese physican who flourished about the middle of the 17th century, and who was one of the first to advocate the great efficacy of cinchona, or Peruvian bark, in the treatment of fevers. He practised medicine at Rome for a certain length of time and then settled in his native city, Genoa. He was in regular attendance at one or more of the hospitals, and he was a member of the Sanitary Council of Genoa.

Bado's first treatise on the subject of cinchona bears the following title: "Cortex peruviæ redivivus profligator febrium assertus ab impugnationibus Melippi protimi belgæ medici," Genoa, 1656. The second one was published seven years later. It bears the title: "Anastasis corticis peruviani, seu Chinæ defensio Seb. Badi, etc., contra ventilentiones Jo. Jacobi Chiffletii, gemitusque Vopisci Fortunati Plempii, illustrium medicorum," Genoa, 1663. In this treatise the author gives the history of the discovery of "quinquina" and of the way in which it was introduced into Europe; he also specifies in what classes of cases the drug will be found useful, etc. Both Torti and Haller speak well of the book.

A. H. B.

Bael Fruit.—The fruit of *Aegle Marmelos* Correo (fam. *Rutaceæ*). The bael is a sacred tree among the Hindus, and its use in medicine pertains largely to religion and mythology. It is a near relative of the orange, to which it bears a general resemblance in tree, flower, and fruit. The fruit, of the size, shape, and structure of an orange and with a somewhat similar pulp, differs in having a hard smooth shell, the pulp mucilaginous, and the seeds enclosed in a woolly covering. For medicinal purposes it is collected and dried in slices, usually in quarters, with the shell retained. In the dried condition the pulp is dry, hard, and gummy, and of a mucilaginous, slightly acid, and somewhat bitter taste. Although it contains no tannin, or any other constituent which might be expected to be medicinal, it has been recommended in diarrhea and dysentery. Possibly the large amount of mucilage which it yields may act as a demulcent. There is no fixed dose.

H. H. RUSBY.

Baelz's Disease of the Lip.—See *Myxadenitis Labialis*.

von Baer, Karl Ernst.—Born at Piep, in the Province of Esthonia, Russia, February 29, 1792. He studied medicine, first at the University of Dorpat, and then at Würzburg. At an early period of his career he devoted himself to the study of evolution. At first he collaborated with C. H. Pander in studies on the development of the chick. Later, he extended his researches to the evolution of organisms generally. In 1817 he was invited by his old teacher, K. F. Burdach, then Professor of Anatomy at Königsberg, to become his prosector and chief of the new Zoological Museum in that city. He accepted the invitation, and continued his researches with renewed vigor. In 1827 he published, at Leipzig, the now famous treatise entitled: "Epistola de ovo mammalium et hominis genesi," a work in which appears for the first time a description of his great discovery of the human ovum. In the

FIG. 612.—Karl Ernst v. Baer.

following year (1828) he published the first part of his larger work, "Ueber die Entwickelungsgeschichte der Thiere." The second part was not published until nine years later (1837). In 1835 von Baer published his treatise on the development of fishes, and in 1837 he was appointed leader of an arctic expedition. The remainder of his active life was devoted to researches in geology as well as in biology. In 1867 he was awarded the Copley medal. He died at Dorpat November 28, 1876.

The writer of the biographical sketch of von Baer in the *Encyclopedia Britannica* speaks of the value of this investigator's contributions to our knowledge of biology in the following terms: "The influence of von Baer's discoveries has been far-reaching and abiding. Not only was he the pioneer in that branch of biological science to which Francis Balfour, gathering up the labors of many fellow-workers, gave coherence in his *Comparative Embryology* (1881), but the impetus to T. H. Huxley's researches on the structure of the *Medusæ* came from him, and Herbert Spencer found in von Baer's 'law of development' the 'law of all development.'" A. H. B.

von Baerensprung, Friedrich Wilhelm Felix.—Born in Berlin, Prussia, March 30, 1822. He studied medicine in Berlin and Halle, and devoted a great deal of attention to syphilis and skin diseases. In 1856 he was made Professor Extraordinary of these two branches of medical science. His death occurred August 26, 1864.

Baerensprung ranks as one of the leading dermatologists of the nineteenth century. He deserves special recognition because he demonstrated the fact that in herpes zoster there are pathological changes in the spinal ganglia. (His paper on this subject is to be found in the Charite-Annalen.) His popularity was still further increased by the fact that—simultaneously with Traube, but quite independently of him—he drew attention to the necessity of ascertaining, in our examinations of patients, the temperature of their bodies. (See articles in "Müller's Archiv," 1851—1852.) A. H. B.

Bagnères-de-Bigorre.—This is a town of about 12,000 inhabitants, attractively situated in the Hautes-Pyrénées, in the extreme southern portion of France, not far from the Spanish border. The town lies in the foothills of the Pyrénées at an elevation of 1,800 feet. The surrounding country is very beautiful and affords many opportunities for pleasant excursions.

The climate is mild and bracing without sudden changes; the atmosphere is clear and pure, partaking more or less of the characteristics of elevated regions; periodic winds traverse the valley, tempering the heat of the warmest days. The mean annual average temperature is 46.5° F., and there are 147 rainy days in the year. The regular season extends from June 1 to October 1, although the place is frequented both winter and summer by the residents of Pau—a health resort in the vicinity—for the purpose of escaping the heat in summer, and enjoying the clear, dry, bright, and slightly frosty days of winter.

The town is picturesque, with a Spanish appearance, clean and cheerful, with a casino, music, shops, an English church, many delightful excursions, and interesting Roman remains. It is a good place for a long or short stay. The accommodations are good and reasonable.

There are three classes of waters obtained and used at this spa: A. Sulphate-of-lime springs with a trace of arsenic; B. sulphur waters; C. cold ferruginous waters. The sulphate-of-lime springs are the characteristic waters of the place and are of a temperature varying from 88° to 122° F. They are used both internally, and externally in the form of baths, douches, massage, inhalation, vapor baths, etc. There are a large number of hot sulphate-of-lime springs; the Source Salies is the hottest and is without sulphur. The water in appearance is clear, odorless, and of an insipid taste. The direct effect of the waters when taken internally is to stimulate the appetite and digestion, increase the excretion of urine, and render more active intestinal and bronchial secretions. The baths are sedative and soothing to the nervous system; render the circulation fuller and more steady, and the respiration more easy.

The maladies for which these waters are principally employed are those connected with the nervous system, such as hysteria, neurasthenia, insomnia, cases of overwork, chorea, neuralgia and anemia, chlorosis, gastrointestinal, cutaneous, and arthritic disturbances depending upon a neurotic cause; catarrhal conditions of the respiratory passages; and uterine troubles. "The dominant indication at Bagnères-de-Bigorre," says Burney Yeo, "is neurasthenia."

The contraindications are acute febrile affections and arteriosclerosis in elderly persons.

There are two bath establishments with all the appliances for the various kinds of baths.

Considering the beauty of the situation, the excellent climate, the charm of the town, and the effects of the waters, one could hardly imagine a more favorable resort for a neurasthenic, or one afflicted with insomnia. EDWARD O. OTIS.

Bahamas.—See *Nassau*.

Bailey Springs.—Lauderdale County, Alabama. POST-OFFICE.—Bailey Springs. Hotel.

ACCESS.—Via the Louisville and Nashville railroad; also by all steamboats on the Tennessee River. Tickets should be taken to Florence, Ala., nine miles distant by carriage or stage. This is one of the old-time Southern health resorts, the springs having been in use for upward of seventy-five years. They are located in a picturesque valley surrounded by a semi-circular range of hills, among which will be found many leafy arcades and rocky nooks. A moss-banked stream a short distance from the springs, known as Shoal Creek, supplies visitors with facilities for boating and fishing. The hotel buildings are comfortable, old-fashioned structures situated on the summit of the hill, about three hundred feet above the level of Shoal Creek. They were overhauled and brought up to modern requirements a few years ago. The springs here are five in number, known as the "Rock," "Freestone," "Soda," "Alum," and "Sour Iron" springs. The most famous of these is the Rock Spring the analysis of which is as follows:

Solids.	Grains per Gallon.
Magnesium	41
Calcium	2 75
Sodium	1 95
Sulphur peroxide	10
Chlorine	1.32
Silica	1 10
Potassium	.19
Carbonic acid gas	6.65
Organic matter	.41
	14 88
Ammonia, free	Traces
Ammonia, albuminoid	.00291

The waters are recommended for renal disease attended by dropsy, for dyspepsia, and for anemia and general debility. They are believed to possess sedative effects upon the nervous system, and in virtue of this action are prescribed in cases of restlessness and insomnia due to alcoholism, overwork and anxiety.

The "Alum" spring has acquired considerable reputation in the local treatment of skin affections, ulcerations, and inflammatory affections of the eye. EMMA E. WALKER.

Baillie, Walter.—Born at Portsham, England, in 1529. In 1558 he was admitted to the practice of medicine by the University of Oxford. In 1561 he was made Regius Professor of Medicine at the same institution. Finally, he was appointed Physician to the Queen. He died on March 3, 1593, and his remains were buried in the interior chapel of the college. One writer speaks of Baillie as "the Esculapius of his time, a physician well grounded in the theory of medicine and very successful in its practice."

The following are the titles of his published writings: "A Discourse of Three Kinds of Pepper in Common Use," 1558; "A Brief Treatise of the Preservation of the Eye-sight," Oxford, 1616 (also 1654); and "Directions for Health, Natural and Artificial, with Medicines for all Diseases of the Eye," 1624.

A. H. B.

de Baillou, Guillaume.—Born in the vicinity of Paris, France, about 1538. He received the degree of Bachelor of Medicine in 1568, and two years later he was given the doctor's cap. He was held in such high esteem by his professional associates that they made him Dean of the Medical Faculty in 1580, and reelected him at the expiration of his term of office. From this time forward Baillou devoted himself with special energy to the treatment of disease and to the collection of clinical data upon which he might base truthful descriptions of the maladies which came under his observation. He possessed considerable independence of character, as evidenced by his refusal to take charge of patients belonging to Court circles. On the other hand, he showed himself ever ready to give a helpful hand to the poor whenever they had need of his professional services or of assistance of any kind. He died in 1616, at the age of seventy-eight.

Gui Patin, a celebrated physician who flourished about 1650, maintained that, aside from Hippocrates and Galen, there were only five medical authors whose published writings he took any pleasure in reading; and Baillou was one of these five. "All the other medical treatises," Patin said, "were feeble copies of these excellent books." Baillou's chief distinction lay in the fact that he was one of the pioneers in the movement to interrogate nature directly and not to continue the harmful practice of following the teachings of the ancients blindly. In his writings Baillou makes it evident that he was a talented observer and a practitioner of wide experience. His writings were not put in print during his lifetime; the manuscripts became the property of his nephews, and they published them from time to time during the years 1635–1650. Here are the titles of a few of the more important of Baillou's works: "Consiliorum medicinalium," in three volumes, Paris, 1635–1649; "Epidemiorum et ephemeridum libri II," Paris, 1640; "De convulsionibus libellus," Paris, 1640; "Opuscula medica de arthritide, calculo et urinarum hypostasi," Paris, 1643; "De virginum et mulierum morbis liber," Paris, 1643; and "Opera omnia," published in several editions from 1635 to 1762.

A. H. B.

Balanites Roxburghii Planch.—(Fam. *Simarubaceæ*.) The bark and fruit of this small tree are ancient drugs of India, where they are used as purgatives and anthelmintics, both for human beings and for cattle. The active principle, or the chief one, appears to be saponin. Oil of Balanites is obtained from the kernels, and is said to be similar to peanut oil.

H. H. Rusby.

Balanitis and Balanoposthitis.—(*βάλανος*, an acorn; *πόσθη*, the foreskin.) An inflammation of the mucous membrane covering the glans penis (balanitis) and of that lining the prepuce (posthitis). This is a purely local affection which occurs very commonly as a complication of the various venereal diseases and, much more rarely, with diabetes mellitus. It has, however, no necessary relation with either, and results more often from other and simpler forms of irritation.

Etiology.—The anatomy of the part is the predisposing cause for this inflammation, the apposing surfaces of the mucous membrane favoring the retention of urine, smegma, or various pathological discharges until they may decompose and serve as irritants for the delicate mucous surfaces. If a prepuce is redundant and phimotic the opportunities for such retention of irritating substances are so much the greater.

Diabetes, rheumatism, and gout also predispose to this disease.

The immediate cause of the inflammation may be the mechanical irritation of friction (chafing of clothing, etc.) or the irritating discharges of syphilitic and chancroidal lesions, and urethral discharges, gonorrheal or non-gonorrheal. Vaginal and uterine discharges introduced under the prepuce during coitus may also serve as the exciting cause of the inflammation. By far the commonest cause, however, is uncleanliness and the consequent decomposition of urine and smegma with resulting irritation, and Fournier says that two-thirds of all cases are caused in this way by simple lack of cleanliness, while the other third is caused by the irritation of venereal discharges.

Symptoms.—In the common and mild type of this inflammation a sensation of heat and itching is usually the first suggestion of trouble. Examination reveals a reddened and swollen membrane and the beginnings of an offensive discharge of a thick creamy character. The intensity of the process is usually greatest in the sulcus back of the corona glandis, as it is there that the discharge has the best opportunity to accumulate. If the disease progresses a stage further, the next result is a series of small excoriations which, together with a more profuse discharge and a much greater swelling of the prepuce (which in its turn results in a more or less complete inflammatory phimosis), completes the picture of the severe type of the disease which often occurs as a complication of syphilis, chancroid, and gonorrhea. Even in these cases the complication is not the result of the activity of the specific germs of these diseases, but is a consequence of the irritating character of their discharges, or of an infection with pus-producing germs contained in them.

The erosions sometimes extend and involve most of the mucous membrane of both glans and prepuce, in which case they are apt to develop a circinate margin which is quite characteristic.

Complications.—Occasionally the process becomes so severe that *gangrene* results unless interference be prompt and effectual. The sloughing process may result in a more or less complete destruction of the prepuce and the formation of considerable cicatricial tissue. Occasionally the glans penis is found protruding through an opening which has sloughed through the prepuce. Such extreme destruction of tissue takes place naturally only in phimotic cases in which operative interference is impossible or is neglected.

An *hypertrophy* of the tissues of both prepuce and glans penis, similar to that seen at times as a result of the long-continued irritation of a rubber urinal, may result in persons who are subject to repeated attacks of balanitis. This hypertrophy is said to occur more commonly in the balanitis which accompanies diabetes mellitus, and the thick, rigid prepuce is often a great mechanical annoyance. It may, finally, assume an epitheliomatous character.

Condylomata frequently develop, most frequently in the postcoronal sulcus, in cases of recurrent balanitis.

Lymphadenitis occurs, but rarely results in suppurating bubo.

Paraphimosis of the thickened and inflamed prepuce is not an uncommon complication.

Diagnosis.—The diagnosis is usually easy except in cases in which inflammatory phimosis exists and a purulent discharge with non-retractile prepuce is present. In such cases a distinct, localized area of induration felt through the swollen prepuce suggests the initial lesion of syphilis, and continued search generally reveals other indications of that disease. Gonococci in the pus establish the gonorrheal origin of the process, while the extent of the inflammation together with its rapid progress and the frequent presence of chancroidal ulcers on the preputial margin will usually serve to indicate the chancroidal origin of the disease. If the prepuce is retractile and the lesions can be seen and examined, the diagnosis is usually simple. The history of the case and the appearance of other lesions usually make the syphilitic origin of the inflammation plain, while the markedly circumscribed character of the erosions (which quickly become typical chancroidal ulcers), together with the greater inflammatory hardness and thickening of the tissues of the glans and prepuce, usually leave no doubt as to the chancroidal character of the process. Erosions due to herpes cannot always be distinguished from those of balanitis, although in most cases some few small, discrete, herpetic vesicles will prove characteristic enough to make the diagnosis clear.

Prognosis.—The prognosis is good, but one should not forget the possibility of the gangrene, which occurs rarely in old and debilitated persons or in those cases in which proper treatment is neglected or is impossible.

Treatment.—The prophylaxis of this inflammation consists in cleanliness. Retraction of the prepuce and daily washing of the subpreputial cavity usually suffice to prevent a recurrence of the trouble.

Treatment of the ordinary type of the inflammation should be carried out about as follows: (1) retraction of the prepuce; (2) a mild antiseptic wash, *e.g.* dilute lead wash or 1 to 5,000 corrosive sublimate; (3) careful drying of the exposed surfaces in such a manner as not to chafe and irritate them; (4) dusting on an unirritating powder such as bismuth, bismuth and calomel in equal parts, thymol iodide (in the chancroidal cases), oxalate of cerium; (5) separating the powdered surfaces of membrane by a very thin layer of absorbent cotton.

If the discharge is profuse and the erosions are extensive it is often of advantage to omit the powder and to substitute a thin layer of absorbent cotton wrapped about the glans penis and then moistened with lead wash or some equally unirritating lotion. Erosions or ulcerations which do not heal readily should be gently touched with a bit of cotton on a cotton carrier slightly moistened with a solution of nitrate of silver—five to twenty per cent. as needed in individual cases.

Phimotic cases are often very troublesome, as their proper cleansing is well nigh impossible of attainment. They should be irrigated very often, in severe cases every hour or two, with warm water followed by mild antiseptic solutions, a large urethral syringe with a blunt nozzle being as convenient an instrument as any for the purpose. Corrosive sublimate solution, 1 to 5,000, carbolic acid solution, 1 to 100, lysol, and creolin are all good irrigating fluids, but the writer does not approve of the use of peroxide of hydrogen in these cases, as it is very irritating and often causes much preputial swelling if used in strength sufficient to make it of much value.

If the disease proves stubborn and there is a probability that the ulcerative process is extending under the tight and swollen foreskin, every effort should be made to reduce the acuteness of the inflammation with hot soakings, etc., and then an operation under the strictest aseptic and antiseptic precautions should be performed, the patient being told that he is not to expect a primary healing. In such cases the dorsal incision of the prepuce may prove adequate to the needs of the case, but more frequently a complete circumcision is necessary. Even in the chancroidal cases the writer has never met with any untoward result from such operative procedures, although primary healing is by no means the rule.

In all cases, however mild, care should be taken in urinating to retract the foreskin sufficiently to lay bare the region of the meatus if possible, so that the urine may pass clear of the prepuce and not contaminate the subpreputial cotton, and so render its very frequent renewal more than ever imperative.

Cleanliness, then, with mild but constantly repeated antiseptic washes, and the dorsal incision or circumcision when needed in severe cases, form the basis of all treatment. Paul Thorndike.

Balantidium.—A genus of *Infusoria* that is sometimes found in man. *B. coli* is found in the intestine, often with diarrhea, and is said even to cause ulcers in the intestinal mucosa. *B. minutum* is found in cases of catarrhal inflammation of the intestine. See *Protozoa*. A. S. P.

Balard, Antoine Jerôme.—Born at Montpellier, France, on September 30, 1802. In 1826 he discovered in sea-water a previously unknown element, and he gave to it the name *bromine*. This achievement brought him considerable fame, and in 1851 he was made Professor of Chemistry at the Collège de France, in Paris. He died in the latter city on April 30, 1876. A. H. B.

Baldness.—See *Alopecia*.

Balfour, Francis Maitland.—Born at Edinburgh, Scotland, on Nov. 10, 1851. He devoted all his attention, after 1871, to original researches in the domain of animal morphology. His first published writing (1878) was a monograph on the Elasmobranch Fishes. His next work was a large treatise on *Comparative Embryology*, in two volumes—the first, published in 1880, deals with the invertebrates, and the second (1881) with the vertebrates. In 1882 Cambridge University made him a special professor of animal morphology. Shortly after he received this appointment he was taken ill with typhoid fever, and it was during a trip which he made to Switzerland for the purpose of regaining his health after this serious illness, that he lost his life (July 19, 1882) in attempting the ascent of one of the peaks of the Mont Blanc group. A. H. B.

Ballardvale Spring.—Essex County, Massachusetts.

Location.—Andover.

Access.—The Ballardvale Spring is about one mile from the railway station at Lowell Junction, Massachusetts. It is within a few feet of good automobile transportation.

The following analysis of the water was made by the Bureau of Chemistry in 1910:

Parts per Million.	
Ammonium chloride	trace.
Potassium chloride	0.49
Sodium nitrate	0.05
Sodium chloride	3.82
Sodium sulphate	1.92
Sodium bicarbonate	0.25
Magnesium bicarbonate	2.88
Calcium bicarbonate	4.54
Ferric oxide	0.10
Silica	7.30
Total	21.35
Gases.	c.c.
Carbon dioxide (free)	1.7
Carbon dioxide (set free from bicarbonate upon evaporating to dryness)	0.9

Temperature of water 40° F.

The water is a very slightly mineralized, sodic, bicarbonated, muriated water of the alkaline-saline type. The spring has a large flow.

The water has been found useful in dyspepsia, rheumatism, prostatic irritation, and the albuminuria of pregnancy. The water is used commercially.

EMMA E. WALKER.

Ballottement.—This term, which means literally tossing, was introduced by Baudelocque to denote the sensation imparted to the exploring finger when the gravid uterus is suddenly forced upward or backward. This sensation is produced by the fetus, a solid body, floating in the amniotic fluid. Pajot likens the sensation to that produced by the finger in striking a piece of ice floating in a vessel of water. When the finger is applied dry to the lump of ice, the latter first slips down into the water, and if the finger be left in position the ice bobs up and strikes it. The first act is termed single ballottement and the complete act double ballottement. A further division is into abdominal and vaginal ballottement, although the latter is commonly implied when the word is in ordinary use.

In abdominal ballottement the element of gravity is not present. A hand is placed against the abdomen, on either side of the uterus, and while one hand is fixed, the fingers of the other are pressed abruptly against the uterine wall. As a rule single ballottement is readily obtained, but the recoil or *choc en retour* is often not forthcoming. Instead of this the opposite or passive hand often feels a counterstroke when the pressure is made. If the fundus has reached the level of the navel, the pressure of the fetal head at this region may be revealed by abdominal ballottement properly carried out. The proper maneuver is to place the right palm against the fundus, while sudden pressure is made against the latter with the finger tips of the left hand previously pressed deeply into the abdomen. Abdominal ballottement may sometimes be obtained as early as four and a half months, but is not clean cut as a rule until the beginning of the sixth month.

Vaginal ballottement can seldom be elicited until after the middle of the fourth month. To obtain it the tips of the index and middle fingers are introduced into the anterior vaginal cul-de-sac, face downward. Velpeau advised that the fingers be placed against the cervix. Pressure is then made against the lower segment of the uterus until the most dependent portion of the fetus is felt. The latter is then suddenly thrust away by the fingers, whereupon it rises in the amniotic fluid. Ordinarily the *choc en retour* is not only tardily perceived but it is also but slightly in evidence. As a rule vaginal ballottement is done with the patient standing or reclining. It may be effected in the lying posture but is less trustworthy.

Ballottement is hardly suited for a universal resource in the diagnosis of pregnancy, for it can seldom be elicited in breech and shoulder presentations and is without value in the diagnosis of twin pregnancy. Since pressure is made in the inferior segment in vaginal ballottement the latter is of no value when the insertion of the placenta is low down in the uterine cavity.

The chief value of ballottement is early in the middle third of gestation, before other pathognomonic signs are in evidence. Hence the earlier it can be obtained, the greater its value. When the test is positive at the fourteenth week, the existence of pregnancy is practically assured, irrespective of the outcome of other tests. But since as a rule it cannot be depended upon until some days after the twentieth week, the diagnosis should have been made by other means by that time. Therefore, it is not of much value in routine work. EDWARD PREBLE.

Ballston Spa.—Saratoga County, New York.

POST-OFFICE.—Ballston. Hotels.

ACCESS.—From Albany viâ Delaware and Hudson Railroad, thirty-two miles north. The location is seven miles southeast of Saratoga Springs. The town is connected with these places by both steam railroad and trolley.

The fame of Ballston Springs is almost coeval with that of Saratoga, and at one time it was a formidable rival of that celebrated resort. Ballston is a very attractive town, where those who wish to avoid the whirl of Saratoga may live quietly and drink excellent mineral waters at the same time. There are two excellent sanatoria in the town. Some of the springs are very heavily mineralized. Following are analyses of four of the most important:

ONE UNITED STATES GALLON CONTAINS:

Solids.	Sans Souci Spring. J. H. Steele. Grains.	Artesian Lithia Spring. C. F. Chandler. Grains.	Comstock, formerly Franklin Mineral Spring. C. F. Chandler. Grains.	United States. L. C. Beck. Grains.
Sodium carbonate	12.66			16.88
Sodium bicarbonate		11.93	94.60	
Calcium carbonate (with iron oxide)	43.41			29.20
Calcium bicarbonate		238.16	202.33	
Magnesium carbonate				5.76
Magnesium bicarbonate	39.10	180.60	177.87	
Strontium bicarbonate		0.87	Trace.	
Lithium bicarbonate		7.75	6.78	
Iron carbonate	5.95			
Iron bicarbonate		1.58	1.61	
Barium bicarbonate		3.88	1.23	
Sodium sulphate				1.76
Sotassium sulphate		0.52	0.76	
Sodium phosphate		0.05	0.01	
Sodium biborate		Trace.	Trace.	
Sodium chloride		750.03	659.34	424.96
Sotassium chloride		33.28	33.93	
Sodium bromide	143.73	3.64	4.67	
Calcium fluoride		Trace.	Trace.	
Sodium iodide	1.30	0.12	0.24	
Alumina		0.08	0.26	
Silica	1.00	0.76	0.74	8.00
Organic matter		Trace.	Trace.	
Total	247.15	1,233.25	1,184.37	486.56
Gas.	Cubic Inches.	Cubic Inches.	Cubic Inches.	Cubic Inches.
Carbon dioxide		4,261.14	460.06	244.00

It will thus be observed that these waters are quite similar to those of Saratoga. Some of them are indeed much richer in mineral ingredients than any of the Saratoga waters. They are all saline, but some of them, as will be seen, are quite heavily impregnated with calcium, iron, and magnesium. The waters are certainly of great value for medicinal purposes, and have proved useful in disorders of the stomach, liver and kidneys; also in constipation, gout, and rheumatism. There are several other well-known springs at Ballston, among them being the Washington Lithia Well and the Iron Spring.

EMMA E. WALKER.

Balm.—This name, as well as various compounds of it, has been applied to so many different plants that its use is altogether indefinite. Only four of these drugs are of any degree of importance, and their descriptions should be sought as follows: For Lemon Balm, to which the term balm is most appro-

priately applied, see *Melissa;* for Bee Balm, see *Monarda;* for Patchouli Balm, see *Patchouli;* for Mountain Balm, see *Eriodictyon.* H. H. Rusby.

Balm, Lemon.—See *Melissa.*

Balm of Gilead.—A resinous exudation or so-called balsam, from the *Balsamodendron gileadense* Kunth (fam. *Burseraceæ*), a small tree of the Red Sea region. It has ordinary aromatic stimulant properties. It is no longer in use, but possesses considerable historical interest. The name has also been applied to our northern balsam fir and its products (see *Canada Balsam*), as well as to the buds of *Populus candicans* Aiton. H. H. Rusby.

Balneology.—The scientific medical study of bathing and medical springs (Oxford Dictionary). Balneology is a part of the larger science of medical hydrology which is that department or division of medical science which treats of the use of waters, especially mineral waters, for therapeutic purposes (Foster's Encyclopedic Medical Dictionary). Hydrotherapy is a term usually applied to the use of ordinary water, not necessarily mineralized, for medical treatment; but of late there is a tendency to enlarge the application of this word so as to include balneology as well.

The history of the science of hydrology, including balneology and hydrotherapy, is most interesting, reaching back to the earliest period of civilization, revealing the most remarkable variations in popularity and relative position in the importance assigned to it in medical practice. The temples dedicated to Æsculapius, the god of medicine, were erected near these springs and they were commonly made the sites of hospitals, medical schools, baths, and resorts for the sick. According to Peale, for five centuries mineral waters were almost the only medicines used in Rome. It is claimed that there were at one time 800 thermæ in Rome some of which were marvels of luxury and their ruins are now among the most interesting relics of the Eternal City. For historical notes see Peale,[1] Fox,[2] and Weber.[3]

To trace this science from rude beginnings to the present would require a volume. The modern student and practitioner is confronted with the most difficult and abstruse questions relating to the chemistry of mineral springs and their physiological action that are almost the despair of those of ordinary scientific training. The chemical analyses of waters on which so much stress has been laid ever since analytical chemistry has been employed to determine their character are now themselves in process of passing into history. A glance at the recent publications of the chemical division of the United States Geological Survey shows how completely the modern chemist has changed his notation to conform with the latest discoveries in the science of radicles, molecules, atoms, and ions. (See Chase Palmer,[4] Talbot, and Blanchard.[5])

An ion is an atom or group of atoms, forming in itself a complete individual, and possessing a charge of electricity; it may be produced by the dissociation of larger electrically neutral molecules (that is, of the molecules of compounds as ordinarily expressed by their chemical formulas) into smaller ones bearing, respectively, equivalent amounts of positive and negative electricity. In every solution the aggregate of charges on the positive ions which it contains must be exactly equalized by the sum of the charges on the negative ions present, otherwise the solution as a whole could not be electrically neutral. There is, apparently, in solutions some specific power in the solvent by virtue of which it is able so to force itself in between the parts of the molecules as to separate them into ions. Different solvents vary greatly in the extent to which they possess this power, water ranking as the most powerful. (See Talbot and Blanchard.[5])

Dr. R. Fortescue Fox,[2] of London, presents this subject clearly: "In all medicinal springs no doubt much importance attaches to the form in which the ingredients are presented in a more or less dilute solution. It would even seem that very dilute waters are sometimes the most active. Water has the power of fluidifying, or rendering motile, the majority of solids. This fluidification, as in the case of vaporization, is associated with a loosening of the mechanical and chemical structure of the particles. This process as applied to salts is described as dissociation. Water further has the property of taking up molecules produced in this manner between its own molecules, rendering them fluid and motile, dissolving them, and increasing their chemical activity. Moreover, these separated particles, or ions, whether basic or acid, carry a positive or negative electric charge and do not exhibit the usual properties of the free elements. In a solution of sodium chloride, for instance, completely ionized, neither the cation (sodium) nor the anion (chlorine) exhibit the properties of these elements in free state. It is noteworthy that the degree of ionization is in proportion to the dilution of the solution. In many medicinal waters it is supposed that the saline constituents are in a state of complete ionization."

We now have some insight into the remarkable effect of waters of low mineralization and can underr stand why the free motility of the particles of matte may be essential to active metabolic processes as has been suggested.

All waters carrying less than 150 parts per million of total mineral matter are considered "low"; over 500 parts, "high"; and over 2,000 parts "very high." Of course low concentrations of powerful radicles like arsenic may be therapeutically very powerful.

Once firmly established in the mind, the ionic form of expression in parts per million or milligrams per kilogram will be found the easiest to comprehend and to calculate and in harmony with that will be the universal methods of stating the composition of waters.

Equivalents for Converting Analyses of Water into Parts per Million.

Parts per	100,000 × 0.7	= grains per imperial gallon (277 cu. in.)
Parts per	1,000,000 × 0.07	= grains per imperial gallon
Parts per	1,000,000 × 0.058	= grains per U. S. gallon (231 cu. in.)
Grains per imperial gallon	÷ 0.7	= parts per 100,000
Grains per imperial gallon	÷ 0.07	= parts per 1,000,000
Grains per U. S. gallon	÷ 0.58	= parts per 100,000
Grains per U. S. gallon	÷ 0.058	= parts per 1,000,000
One part per hundred (percentage)		= 10,000 parts per million
One part per thousand		= 1,000 parts per million
One gram per liter		= 1,000 parts per million
One milligram per liter		= 1 part per million
One grain per U. S. gallon		= 17,118 parts per million
One grain per imperial gallon		= 14,261 parts per million

The definition of a mineral water varies with the point of view of the chemist, the geologist, the physician, and the dealer. Each has his standard and no arbitrary line depending on total content of minerals or salts in solution can be drawn between so-called pure waters and those commonly denominated as mineral waters. Indeed the most popular and commercially valuable "mineral" water in America has almost a minimum of solid constituents.

In what form and in what combinations the simplest salts exist in mineral waters or in artificial solutions demands the most serious attention. Take, for example, pure water and add to it sodium chloride and potassium sulphate; we have instantly formed in solution sodium sulphate and potassium chloride in addition to the two original salts as well as the sodium, potassium, chloride, and sulphate ions. So the chemists tell us. The electrolytic dissociation theory goes

farther and gives us an entirely new conception of the relation of radicles or ions in various solutions.

An inkling of the state of the radicles of salts in solution is given in what chemists in later years have been stating as the "hypothetical combinations" appended to their analyses so as to correlate them with the time-honored method of notation.

In the past we have been furnished with data of the most diverse kinds. Crook[10] after an inspection of about 1,000 analyses noted that at least forty-two methods of stating the results have been employed. They are all likely now to be superseded by the ionic form which assigns weights directly to the chemically active parts of the dissolved substances instead of using those parts to build imaginary structures (C. Palmer). The sooner we adopt a value of milligrams per liter, or parts per million, discarding the historic "gallon" and think only of radicles instead of salts we shall make a great advance and put ourselves in harmony with modern nomenclature.

For a comparison of these methods take the analysis of sea water, a mineral water of the widest distribution.

Ocean Water.

Amounts Assigned to Hypothetical Combinations.			Amounts to Radicles.	
Combinations.	Milligrams per liter.	Grains per U. S. gallon.	Radicles.	Milligrams per liter.
Sodium chloride (NaCl)....	27,215	1578.4	Sodium (Na).....	10,710
Magnesium chloride ($MgCl_2$)	3,807	220.8	Potassium (K)	390
Magnesium sulphate ($MgSO_4$)	1,658	96.1	Calcium (Ca)	420
Calcium sulphate ($CaSO_4$)	1,260	73.0	Magnesium (Mg)	1,300
Potassium sulphate (K_2SO_4)	863	50.0	Sulphate (SO_4) ...	2,700
Magnesium bromide ($MgBr_2$)	76	4.4	Chloride (Cl).....	19,350
Calcium carbonate ($CaCO_3$).....	121	7.0	Bromide (Br).....	60
			Carbonate (CO_3) ...	70
	35,000	2029.7		35,000

The classification of mineral waters has been attempted by many men of many minds but we believe we owe to Dr. A. C. Peale, of the Smithsonian Institution, Washington, the best and most comprehensive classification which he first presented in a paper read before the American Climatological Association in 1887. He has classified all the mineral springs of the United States that have been analyzed and he has found it to meet the requirements in every case.

All mineral waters are divided into two great groups and are then treated precisely alike with reference to their chemical contents. Group A, *cold* (non-thermal) *springs*. Group B, *thermal springs*. A spring is "thermal" when its temperature is above the mean annual temperature of its locality; it is "cold" when below that temperature. A spring, therefore, might be thermal in Alaska when a spring having an identical temperature would be cold in Virginia.

Class 1. Alkaline { Sulphated. Borated. Muriated.

Class 2. Alkaline-saline { Sulphated. Borated. Muriated.

Class 3. Saline { Sulphated. Muriated.

Class 4. Acid { Sulphated. Muriated. Silicious.

Class 5. Neutral or indifferent waters.

The existence or non-existence of gaseous contents may be shown thus: (1) Non-gaseous: (2) Carbonated (containing CO_2): (3) Sulphureted (containing H_2S); (4) Azotized (having nitrogen gas); (5) Carbureted (having carbureted hydrogen); (6) Radioactive waters.

There may be a combination of gases indicated by the term sulphocarbonated, etc.; we may also carry the subdivision further and according to the predominant basic radicle term the water, sodic, lithic, potassic, calcic, magnesic, chalybeate (containing iron), aluminous, or in combinations as "calcic, magnesic," etc.

Alkaline Waters.—These may be termed sodic, sodic-magnesic, alkaline-chalybeate, or calcic. Alkalinity may be due to sodium, potassium, or lithium (primary alkalinity); or it may be due to the presence of alkaline earths, calcium and magnesium (secondary alkalinity). The term "primary," in this connection, indicates an association with the alkalies of the oldest rock formations of which the alkalies are the principal soluble decomposition products. The alkalinity of waters due to contained calcium and magnesium is termed "secondary" because they occur in connection with rocks of more recent or secondary (stratified) formation. Springs of this class commonly contain carbonic acid gas which increases palatability and solvent power; they also merge by gradation into the succeeding classes, alkaline-saline and saline. Some of the notable alkaline springs in the United States are: the Navajo spring at Manitou, Colorado; Ukiah Vichy, California, and California Seltzer; Waukesha Springs (White Rock, Clysmic), Wisconsin; Londonderry Spring, New Hampshire.

These waters stimulate the action of the stomach and check acidity and fermentation; they increase the urine and lower its acidity and have a good influence on the mucous membrane of the entire digestive tract. Hence they are used in the treatment of acid dyspepsia and flatulence. They are useful in chronic gastric catarrh with hyperchlorhydria, rheumatism, and gout.

Diabetes was at one time supposed to be favorably influenced by the alkaline waters and even yet patients suffering from this complaint are commonly sent to Vichy or to Carlsbad. This mode of treatment arose from the view put forward by Mailke that the disease was due to incomplete oxidation of sugar owing to lack of alkali in the blood. This doctrine has long since passed away, but the practice founded on it still survives. Many patients are, in reality, much benefited by a course at Vichy or at Carlsbad; but there is every reason to believe that this is due not to the waters but to the careful regulation of the diet. The alkaline salts have been shown by many observers to have no power to diminish the formation of sugar, while in all cases the copious administration of water is injurious. Unless alkalies are called for on some independent ground they should not be given in diabetes. (W. R. Huggard.[6])

Lithic Alkaline Waters.—It used to be believed, and spring owners never failed to claim, that there

are wonderful virtues in the lithium waters of this class. The advertised analyses showed as high as twenty-two grains per gallon of carbonate of lithium in one case and absolutely fictitious amounts in many cases. The U. S. Government has put a stop to this and the word "lithia" does not now appear on so many mineral water labels as formerly.[7] It is not proved that lithia has any therapeutic effect very different from its congeners, sodium and potassium. "Lithium appears in several alkaline waters, but in such minute quantities as to have no therapeutic value. The form in which it usually occurs is, moreover, the chloride which is devoid of solvent action on uric acid and its compounds." (W. R. Huggard.[6])

The waters of Carlsbad in Austria, Fachingen in Germany, and Vichy in France are notable examples of the alkaline waters.

Calcic-Magnesic Alkaline Waters.—The waters of secondary alkalinity, or those containing notable amounts of calcium and magnesium, are commonly denominated calcareous waters. They contain a notable proportion of the alkaline earths belonging to the secondary geological formations. The salts of calcium are sparingly soluble in water and give it a characteristic usually termed "hardness." Waters of excessive hardness are entirely unsuitable for drinking but this quality does not prevent their use for bathing. Most of the thermal springs of Virginia and West Virginia belong to this class, the strongest or hardest being used for the baths and those of weaker character being used internally. The Warm Springs, Hot Springs, and Healing Springs of Virginia are in the same valley where limestone belonging to the Silurian and Cambrian (Valley Limestone) formations underlie the surface. These thermal springs range in temperature from 84° to 106° F. and have been used since Revolutionary days for bathing and internal use. The Healing Springs water, which is principally used internally, contains calcium bicarbonate as its principal mineral, analyses showing 356 parts per million or 356 milligrams per kilogram (20.7 grains per gallon). Calcium sulphate is absent. This absence of calcium sulphate is a great advantage, as indigestion and constipation are less likely to be caused. In this respect Healing Springs water bears a close resemblance to those of Wildungen. The waters used for bathing, those coming from the Boiler spring at Hot Springs, are too hard for internal use.

One of the notable discoveries of the last century was made by Thomas Clark, of England, who, in 1841, patented a process for removing the objectionable constituents of hard water. He discovered that ordinary lime water precipitated the soluble calcium bicarbonate as calcium carbonate and that all the calcium was removed simultaneously from the water so treated and from the reagent as well. This process has been of immense value industrially and hygienically and has been widely employed.[4]

Ocean water contains an excessive amount of calcium and magnesium, not altogether dissociated from the chlorine, amounting in all to 420 parts per million for calcium and 1,300 parts for magnesium; the carbonate content in this case is 70, the chlorine content amounting to 19,350.

Calcic, or calcareous, waters, when not associated with chlorine or the sulphate radicle, have a beneficial effect in cases of gout and rheumatism and in counteracting hyperacidity of the stomach and urinary tract. The calcium salts are excreted by the intestine in the form of a phosphate and so the latter's transference to the kidneys and urine is prevented. Von Noorden has shown that the total amount of phosphates in the urine is diminished and as the reaction of the urine approaches alkalinity, the proportion of disodium to monosodium phosphates is modified in favor of the former.

Most of these waters contain, in the natural state, carbonic acid gas and therefore are best used at their source. Calcium salts are eagerly sought by the acids of imperfect digestion. The latter readily combine with the bases thus furnished, and probably in this manner obviate union with similar bases found in bone, cartilage of joints, and in other natural tissues of the body. A proper selection of food is usually enjoined at spas for treatment of rheumatism and gout, in which vegetables rich in salts are recommended so that diet goes hand in hand with mineral waters in the treatment of these affections.

Calcic and magnesic waters favorably influence rheumatism of a subacute or chronic type, pyelitis from kidney concretion, chronic gonorrhea, and bronchial catarrh. They probably also favorably affect scrofulosis, rachitis, and osteomalacia as they supply the deficient salts.

Very recently attention has again been called to the need of lime salts in the treatment of tuberculosis. It is claimed that lime starvation should be corrected by dietetic methods and in this way calcareous waters should have a prominent place. (Van Gieson.[8])

There are valuable thermal calcareous springs in the mountains of Virginia, West Virginia, and Arkansas, some of them almost entirely free from sulphureted hydrogen. There are valuable cold sulphureted calcic-magnesic sulphated alkaline-saline waters at Richfield and Sharon, New York. The waters of Bedford Springs, Pennsylvania, of Contrexéville, France, and Leuk, Switzerland, are non-gaseous calcic, sulphated waters.

Saline Waters.—This large and important class presents all gradations from the weaker alkaline salines to the strong brines. They may contain large quantities of hydrogen sulphide (H_2S) or carbon dioxide (CO_2). Like the alkaline waters they may be referred to as having primary salinity (Na,K) or secondary salinity due to the presence of the calcium and magnesium (earths) and the stronger acid radicles. The term "tertiary salinity" is used to represent acid waters in which the percentage values of the strong acids present are greater than those of the alkalies and earths.

Well-known examples of saline waters are those of Mount Clemens, Michigan; Glen Springs, Saratoga Springs, Clifton Springs, Columbia Springs, New York; Caledonia Springs, between Montreal and Ottawa, Canada; Byron Springs, Eureka Springs, and Calistoga Springs, California. These show a large amount of chlorides and are therefore called "muriated salines." Another large division is called "sulphated saline" because of the predominance of the sulphate radicle. They contain magnesium sulphate (Epsom salt) and sodium sulphate (Glauber's salt) or their respective radicles. Other bases such as calcium and iron are also commonly associated; likewise large quantities of hydrogen sulphide.

The salines have an important place therapeutically on account of their laxative or purgative properties. They have an immense commercial value and although in the United States there are large numbers of these springs whose waters have been extensively sold for a hundred years we nevertheless import vast quantities from Europe. The importation and sale of saline waters of the sulphated variety includes well-known Hunjadi, Apenta, Rubinat, Carabaña, Seidlitz, and Friedrichshall.

It should be noted that in the Saratoga waters, for example, there is more lithium than in so-called lithia waters; the preponderance of the sodium chloride, however, determines the character of Saratoga waters, such as Congress and Hathorn, as saline and they are used accordingly. The chloride of magnesium in saline waters is a constituent of the Mütterlage of salt works; it is present in the Dead Sea and in the stronger brines of Michigan and New York. Potassium chloride and calcium chloride are of no great advantage, as such, when taken internally although

the former is credited with increasing the flow of bile and improving the appetite. It is doubtful if we can differentiate any effect from these lesser constituents when using waters in which other elements greatly preponderate.

The use of sodium chloride waters undoubtedly causes an increase in the flow of gastric juice, bile, pancreatic juice, and intestinal fluid; the appetite is usually increased and the whole digestive tract freshened. There is little opportunity for intestinal putrefaction, fermentation, or autointoxication from the alimentary canal when these waters are faithfully and judiciously used. The chlorinated waters have some advantages over the sulphated waters, or bitter waters, in the case of thin persons whose portal circulatory system is supposed to be sluggish. They correct atonic dyspepsia, furred tongue, bad taste in the mouth and, as noted, almost always improve the appetite. This is the secret of the immense popularity of Saratoga Springs in the earlier days; those who went there to drink the waters were well rewarded and we trust that we may see that spa restored to its former sphere of usefulness.

The waters of French Lick, in their concentrated form, are likewise purgative and depend on the presence of sulphates.

Saline waters have long been employed externally for rheumatic and gouty affections; in connection with carbon dioxide they are used very extensively for the treatment of cardiac diseases. The plan of treatment afforded at Nauheim in Germany where the brothers Schott met with remarkable success, has been adopted at other European spas and has been imitated with more or less success by artificial means. The great advantage which Nauheim has lies in the immense quantity of water containing carbonic acid gas in connection with chlorides and in the proximity of the salt works where a strong brine, or mütterlage, is available for use in baths. Last, but not least, the physicians of the place have developed a plan of treatment suited to a large number of patients presenting a group of symptoms of cardiac and circulatory disturbances. Constant experience in a given class of cases is a great aid in adapting the treatment to individual needs.[9]

Iron, or Chalybeate, Waters.—"Steel" waters of Europe. Iron is found very frequently in mineral waters and in all of the four principal classes. We may have an alkaline chalybeate; an alkaline-saline sulphated chalybeate; an alkaline-saline muriated chalybeate, and an acid sulphated or muriated chalybeate.

There are no absolutely pure chalybeate waters but the iron exists in connection with the bicarbonates, sulphates, chlorides and with other metals such as calcium, magnesium, and aluminum. They are thermal or non-thermal and are associated with free carbonic acid gas and hydrogen sulphide. A water containing bicarbonate of iron is usually preferable for continued use as a tonic to one holding sulphate of iron, as the latter is more astringent.

Free sulphuric acid and alum salts render some iron springs unfit for use; but where these constituents are in moderate quantity and may be taken at their source the effect is often beneficial. A relaxed mucous membrane with a tendency to diarrhea and anemia may be treated successfully with a water of this type. Good examples are Rockbridge alum water, Virginia, or the Oak Orchard Springs, New York.

For continued use in anemia and chlorosis we naturally choose a water with bicarbonate of iron, from a cold spring with an abundance of carbonic acid gas. In the United States we have Berkeley Springs, West Virginia; "Round" Spring at Aurora Springs, Missouri. Those of Spa in Belgium, Schwalbach, in Germany, and St. Moritz in Switzerland. These waters contain respectively 109 parts, 95 parts, and 47 parts per million (in each gallon 6.4, 5.6, and 2.8. grains) of bicarbonate of iron. They are agreeable to take by reason of the large amount of carbonic acid gas present.

English chalybeate spas include Tunbridge wells in Kent and Flitwick Well in Bedfordshire. The Flitwick water contains 2,428 parts per million of sulphate of iron (170 grains to the gallon) and is bottled for sale. The waters of Harrogate and Buxton also contain iron; the so-called "Kissingen" well, one of the eighty springs of Harrogate, contains about ten grains of bicarbonate of iron per gallon; while the "Chloride of Iron" well contains 227 parts per million (13.3 grains of chloride of iron per gallon) and 191 parts per million (11.2 grains per gallon) of bicarbonate of iron. The waters of these chalybeate springs of Harrogate are bottled after being artificially charged with carbonic acid gas. At Harrogate they are generally taken after being heated.

Waters containing bicarbonate of iron require great care in bottling as most of the iron is liable to be deposited on the sides of the bottle in the form of an insoluble oxide. To prevent this the waters must be sterilized to prevent the growth of any microbes; they must be thoroughly charged with carbonic acid gas and be very carefully closed. Chalybeate waters always give the best results when taken directly from the spring.

One reason why the iron waters do not act so well after bottling is that if much lime is present, as is frequently the case, the iron precipitates. The waters of Schwalbach, on that account, keep better than those of Pyrmont which contain lime in abundance. Those from the Prince de Condé Spa keep the best of all and may be given in quantities of from one to four tumblers a day. They aid digestion and improve the quality of the blood.

Iron waters are best taken after meals in quantities varying from four to eight ounces. The use of eight ounces may produce headache in susceptible patients. It is best to order a saline water before breakfast when giving iron waters.

The waters of Franzenbad, Marienbad, and Kissingen (Rakoczy) all contain some bicarbonate of iron and are bottled for use. Iron springs are rather common in the United States. One of the purest chalybeate springs gives the following analysis:

"Round" Spring, Aurora Springs, Missouri.

	Parts per million.	Grains per U. S. gallon.
Ferrous carbonate	87.8	5.13
Ferrous oxide	15.9	0.93
Magnesium chloride	118.9	6.95
Sodium chloride	68.6	4.01
Calcium sulphate	41.4	2.42
Lithia	24.4	1.43

Iron Salts.

	Parts per million.	Grains in one gallon.
Cresson Springs, Pa., Iron spring	487.8	28.5
Cresson Springs, Pa., Alum spring	763.4	44.6
Mardela Spring, Md.	196.8	11.5
Rock Enon Springs, Va.	243.0	14.2
Massanetta, Va.	53.0	3.1
Napa Soda Springs, Cal.	135.2	7.9
Topeka Mineral Well, Kansas	481.0	28.0
Matchless Mineral Water, Ala.	17,973.0	1,050.0

Chalybeate waters are useful in anemia, general debility, and scrofula. The more astringent waters may be chosen in cases of chronic diarrhea and in

malarial cachexia. Iron waters are generally deemed unsuitable in any case of fever, in gastric irritability and in pulmonary diseases only if hemorrhage is a feature. Like most mineral waters they are diuretic. If associated with a little arsenic or manganese their value is probably enhanced.

Arsenic Waters.—Waters of this class are found in the United States and Europe, the best known being as follows:

	Parts per million.	Grains of As per gallon.
Mont Dore, Puy de Dome, France	11.9	0.7
Levico, Austrian Tyrol, Strong	10.2	0.6
Roncegno	3.9	....
Crockett Arsenic Lithia Spring, Montgomery Co., Va.	2.4	0.14

These waters contain iron as sulphate. The small quantity of arsenic acid or arsenous salts is readily taken up in the blood stream and increases the amount of hemoglobin. Arsenic has an effect on the skin which seems to be better nourished. According to the investigations of Schultz and Binz the process of transformation of arsenous acid into arsenic within the body may possibly cause a to-and-fro movement of the oxygen atoms in the protoplasm which, in connection with the direct effect of small doses of arsenic, stimulates the processes of tissue formation.

Gaseous Waters.—The presence of gases, such as nitrogen, carbon dioxide, or hydrogen sulphide, adds a distinctive character to mineral waters and sometimes suggests the name of the spring. It is a well-known fact that the estimation of gases in mineral waters is quite uncertain, varying more than in the analyses of solid contents by different chemists. Gases are, naturally, volatile and must be estimated at the spring and even then the results vary greatly. The fact that waters are released from all pressure on their emergence at the springs determines the escape of the contained gas. This has led to some very interesting questions and, incidently, to lawsuits. These hinged on the point whether a water was still natural when the original gas had escaped and when the gas, or other similar gas, has been recombined with the water under artificial pressure. Natural waters were formerly admitted free of duty into the United States and artificial waters were taxed. The famous case of the U. S. Government *vs.* the Apollinaris Co. was decided after much litigation in favor of the latter.

It should be remembered that a given quantity of water, *e.g.* one liter of water at 15° C. and at the ordinary atmospheric pressure, can contain the same volume, one liter of carbonic acid gas; but to contain five times that bulk it must be subjected to a pressure of five atmospheres. In the case of hydrogen sulphide, at 15° C. and at atmospheric pressure, as much as 3.24 volumes can be contained. Heating, however, in all cases speedily reduces the percentage of gas contained and hence it is that cold gaseous springs are usually more highly charged than hot gaseous springs. Practically, all carbonated waters when bottled for sale are artificially charged. All mineral waters should be taken as fresh as possible. If bottled waters are used the best of corks should be used and if this point is neglected the water is liable to deteriorate, lose its proper taste, and may be positively dangerous. Hence waters should be purchased from a large dealer whose stock is never allowed to deteriorate.

Radioactive Waters.—Professors B. B. Boltwood and J. H. Pratt, of New Haven, have tested a large number of mineral springs for radioactivity. Of the waters of Hot Springs, Arkansas, they report forty-four radioactive to a marked degree; this is due to dissolved radium emanation (a gas) and not due to the presence of salts or other radioactive solids; the tufa deposited by the springs does not contain any appreciable traces of radium. Radioactivity is a quality lost very soon after bottling.

We should endeavor to cultivate a rational use of mineral waters and a true knowledge of their contents and physiological action. The majority of people depend on the advertised analysis of waters and the statements of their owners, or their agents, regarding their action on the system. Others rely upon personal experience at the fountain-head or on physicians who have studied their effects. The empiric method and the scientific investigation should go hand in hand. The United States Government and the French Government through the "Commission des Eaux Minerales" of the Académie de Médecine have taken this matter in hand. For the past twenty years no mineral water can be advertised as such or can a mineral water station be exploited in France without the favorable recommendation of the commission under whose direction the analyses are made. Such a guarantee of accuracy has been lacking in the United States until recently. It needs only a glance at the U. S. Government report on Lithia Waters to see what absurd claims were made by mineral spring owners as to the amount of lithia contained when the U. S. Government chemists showed that the lithia content in many cases was inappreciable.*

Although there is a widespread belief in the specific action of mineral waters when used for bathing there is no scientific basis for the supposition that any of the mineral contents are absorbed through the uninjured skin when the body is immersed. This subject is a large and important one and has been the subject of most careful observations in Germany and Austria.[9] The beneficial action of mineral waters when externally used depends on the action on the peripheral nerves or end organs of the skin and, by them, on the central nervous system; and on the thermic stimulus in connection with the physical force used in the applications. The thermic stimulus is succeeded by a reaction which, in most cases, is brought about when the waters are properly applied. The body reacts to heat or plus (hyperthermal) stimulations, and to cold or minus stimulations. We can thus heighten innervation, lower or abolish it at the point of application, or in the central organs, or by reflex processes in the most varied motor and vasomotor tracts. As Winternitz puts it: "Thermal stimulations are therefore indicated when innervation requires to be strengthened, suspended, or altered." He assigns in this class of effects the first place to the action of baths on the vasomotor center. This is the key to the action of baths in fever.

Balneology includes not only the internal administration of waters but also baths in mineral springs. These uses of waters are almost always associated and different observers from time immemorial have attached different values to these two therapeutic methods. At most spas both modes are utilized. Their combination in a given case usually gives the best results. At resorts like Saratoga the internal use of the spring waters takes precedence, while at Mount Clemens, Michigan, White Sulphur Springs, West Virginia, and Nauheim in Germany baths are chiefly relied upon. At Hot Springs, Virginia, French Lick, Indiana, Carlsbad, Austria, and Aix-les-Bains and Vichy in France the combined method prevails. It is rather significant that in the three

* Lately the United States Government has undertaken a thorough investigation of the chemical and medicinal properties of the waters of Hot Springs, Arkansas, where there are two government hospitals and where the entire property, including the springs belongs to the United States. This commission involving an outlay of $50,000 will probably be authorized by the present Congress.

great resorts for the treatment of gout and rheumatism in the United States these affections have been treated with great success for many years with baths of widely different character. Take, for example, the analyses of waters at Hot Springs, Virginia, Hot Springs, Arkansas, and Mount Clemens, Michigan. The latter baths have over one thousand times as much solid contents as the Arkansas baths and eighty thousand times as much common salt. The Arkansas Springs have half as much calcium bicarbonate as the Virginia Hot Springs. Neither contain iron, while the Mount Clemens baths are rich in iron.

Analysis in parts per million, Hypothetical combinations.	Hot Springs, Arkansas. Big Iron Spg.	Hot Springs, Virginia. Boiler Spg.	Mt. Clemens, Michigan. Park Baths.
NH_4Cl	0.119		
KCl	3.050	9.3	12,500
NaCl	1.650		112,482
$MgCl_2$			25,743
$CaCl_2$			125,800
$NaSO_4$	10.06	63.0	
$MgSO_4$	1.30	146.0	
KSO_4		11.5	
$MgBr_2$			1,176
$NaBO_3$	1.98		
$Mg(HCO_3)_2$	20.10	52.0	
$Ca(HCO_3)_2$	190.00	397.0	
$FE_2O_3+Al_2O_3$	0.27		
FE_2O_3			495
$Mn(HCO_3)_2$	1.09		
SiO_2	45.60	33 5	2,490
$CaSO_4$		33.0	18,103
Total solids	284.88	745.3	298,789
Gases. CO_2 Cubic inches	1.6	24.6	3.5
H_2S per gallon	0	0	10

If we assume that approximately equal results are achieved by a course of bathing in waters so dissimilar we cannot avoid the influence that the chemical constituents of these different springs are not *per se* the active therapeutic agents. That certain baths should be used for a case of syphilis and the same for a case of gout with good results ought to suggest that the hydrotherapeutic or balneological methods employed are more potent than the fact that the waters employed have a special chemical analysis. The differentiation of mineral springs for therapeutic purposes has some practical basis; but we believe it has been carried too far, especially in European practice.

GUY HINSDALE.

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Balsamum Peruvianum.—*Balsam of Peru.* "A balsam obtained from *Toluifera pereiræ* (Royle) Baillon (fam. *Leguminosæ*)." (U. S. P.) This is a good-sized tree, with a dark, smooth trunk, branching near the ground. It attains often a height of sixteen or eighteen meters (52 to 58 feet), and resembles, in its botanical characters, *T. balsamum*, described in the succeeding article. It is a native of Central America, and protected, but not really cultivated, as a source of the balsam, in the Indian reservation lands of San Salvador, along the Balsam Coast. It is has been introduced into Ceylon, where it flourishes vigorously.

Balsam of Peru was one of the earliest products carried to the Old World from Central America, and was at first extravagantly prized for its medicinal properties, as well as for its use as incense in the Catholic churches. It was at first exported indirectly, by way of more southern South American ports, and by this means it received its misleading name of balsam of *Peru*. None genuine is now, or ever has been, produced in Peru.

The collection is made in November or December, at the end of the rainy season, when the bark is full of resin. The Indians, to whom the trees belong, then beat the trunks on four sides with the heads of their axes, or with hammers, so as to bruise four strips of bark, and leave as many similar ones untouched. After a few days, they scorch or ignite the contused surfaces with torches, which serves to increase the flow of resin, and then, waiting another week, tear off the loosened strips of bruised bark and swathe the stems in rags, to absorb it. When the cloths are saturated, they are boiled in a vessel of water, and the balsam melted out of them collects in the bottom, and is easily separated. The following year the remaining portions are similarly treated; and in the second year those operated upon first; so, by judicious treatment, a continuous annual yield is obtained for a number of years.

Balsam of Peru is a dark, thickish liquid, looking at a little distance like dark molasses; it does not draw out into a thread and is not sticky; when shaken up upon the sides of a containing glass, the thin layer so obtained is yellowish or reddish-brown and transparent. Its specific gravity is 1.140 to 1.50 at 15° C A specific gravity of 1.140 or higher will exclude the more important adulterants. It has a rather smoky, but not unpleasant, balsamic and slightly vanilla-like odor and a taste which, at first mild, becomes later, in the fauces, warm and acrid. It is insoluble in water, yielding to it only a little free cinnamic acid, but mixes freely with chloroform and absolute alcohol. It does not dry or undergo much change upon exposure to the atmosphere, and should contain no fat. Thirty per cent. of it should dissolve in benzin. An artificial mixture is now largely sold in this country as "synthetic" Balsam of Peru, and much that is sold as genuine contains an admixture of more or less of the artificial.

The composition of the balsam is not very simple, but the principal constituents are: (1) not more than thirty-two per cent. of a resin insoluble in carbon disulphide, and which may be separated by means of that agent; (2) nearly sixty per cent. of cinnamein, a brownish, aromatic liquid (benzylic cinnamate, which this is supposed essentially to be when pure, is really a crystalline solid); (3) traces of cinnamic and benzoic acids and more or less styrol and styracin. Additional amounts of benzoic and cinnamic acids, with styrol and toluol, are obtained on dry distillation. Benzoate of benzyl also occurs in varying amounts. At least sixty-five per cent. should consist of aromatic substances. Balsam of Peru has no specific physiological action. It is a mild carminative and diffusive stimulant, and acts as an antiseptic, especially in excretion through the urinary passages. Locally, it is mildly parasiticidal, and it acts as a disinfectant and stimulating application to wounds and ulcers which lack a disposition to heal. For the latter purpose, a ten per cent. solution in castor oil or vaseline is used. Travelers in tropical South America com-

monly carry the balsam and apply it freely to fresh wounds. The dose is ♏ x. to xxx. (0.6 to 2.0.). There is no official preparation. The volatile oil, distilled off, is an article of commerce used in perfumery.

HENRY H. RUSBY.

Balsamum Tolutanum.—*Balsam of Tolu.* "A balsam obtained from *Toluifera balsamum* L. (fam. *Leguminosæ*)." (U. S. P.)

This is a fine, large evergreen tree, with a tall, straight stem, often rising from thirteen to nineteen meters (forty to sixty feet) without a branch, then bearing a fine round crown. The leaves contain abundance of fragrant oil, the branches and stem are filled with oil and resin. It is a native of Venezuela and New Granada. The balsam has been exported from the latter state since the middle of the sixteenth century. It is collected by the Indians, and was already an object of value among them when the country was discovered. Deep V-shaped incisions are made in the trunk, and at or below the point where they meet a vessel is fastened to receive the exudation. These receptacles are usually calabashes or gourds, and many such may be arranged at the same time around the stem of a large tree. As they become filled, they are emptied into leather bags, in which they are carried to the market or town, and there again they are at present usually emptied into tin cans for exportation.

It is a soft brown, resinous substance, when fresh sometimes thin enough to pour; usually soft enough to be dipped out with a spoon or spatula, but upon exposure becomes harder and finally brittle, although easily softened by warmth. It has a brown color, but in thin layers is yellowish, and either transparent or cloudy, by the deposition of crystals of cinnamic acid. The odor is delicate and very pleasant, recalling that of Siam benzoin, and improves with age. The balsam is almost insoluble in water, but freely soluble in alcohol and chloroform. Its most important constituent is benzyl benzoate, a volatile oil, but solid at a temperature below 20° C. There are also some benzyl cinnamate, traces of cinnamic and benzoic acids, and a variable amount of resin, usually nearly ninety per cent. About one per cent. of a volatile oil (tolane) is obtained upon distilling with water. The resin can be separated into two resins by treatment with alcohol.

The medicinal qualities of tolu are even less marked than those of Peru balsam, as the acrid quality of the latter is almost wanting in the former; still it is very much the more in use, on account of its pleasant odor and taste. It is usually called expectorant, etc., and is a common ingredient in cough mixtures, but in a form which is medicinally wholly inert, further than for a passing local effect upon the fauces. If given with any expectation of modifying the bronchial surfaces, it must be in doses of not less than gr. xv. to xxx. (1.0–2.0) or, probably, better by vapor. Of the preparations, the syrup has a strength of one per cent., and this consists of the oil and crystallizable acids only, not of the resin. It is simply a vehicle. The tincture, *Tinctura Tolutanum*, U. S. P., strength ten per cent., represents the entire balsam, but contains a large dose of alcohol in addition to the medicine in question. In the compound tincture of benzoin (*Tinctura Benzoini Composita*, U. S. P.) it is a subordinate adjunct. So the best ways to give the balsam internally and alone are by pill or an emulsion extemporaneously made. Both this and the preceding balsam are used in toilet soaps and for similar purposes, as perfumes, etc. HENRY H. RUSBY.

Baltimore.—The chief city of Maryland, with a population of 558,785. It is picturesquely situated on the north branch of the Patapsco River, 14 miles from its entrance into Chesapeake Bay, and about 200 miles from the ocean. It is a large manufacturing and commercial center, and has a capacious and safe harbor. It is the seat of the great Johns Hopkins University and Hospital, is well built, and has a large park of 680 acres (Druid Hill Park). It is about 40 miles from Washington and 100 miles from Philadelphia. It is said to be a very healthy city, and has a mild climate, as the following table indicates:

CLIMATE OF BALTIMORE, MD., LATITUDE 39° 18′, LONGITUDE 76° 37′. PERIOD OF OBSERVATION, 13 YEARS; ELEVATION OF PLACE OF OBSERVATION ABOVE SEA LEVEL, 14 FEET.

Data.	January.	July.	Year.
Temperature—Average mean or normal.	34.6° F.	78.5° F.	55.5° F.
Average daily range	13.5° F.	16.8° F.	
Mean of warmest	40.5° F.	86.8° F.	
Mean of coldest	27° F.	70° F.	
Highest or maximum	71° F.	99° F.	
Lowest or minimum	6° F.	59° F.	
Humidity—Average mean relative	70.8%	64.3%	66.4%
Precipitation—Average in inches.	3.05	4.06	41.98
Wind—Prevailing direction	N.W.	S.W.	N.W.
Average hourly velocity in miles.	5.5	5.6	5.8
Weather—Average number of clear days.	7	9.2	108
Average number of fair days	13.2	14.5	151.7
Average number of fair and clear days.	20.2	23.7	259.7

Explanation of Temperature.—The average mean or normal temperature is deduced from the mean temperature of individual months, obtained from three daily observations, viz., at 7 A.M., 3 P.M., and 11 P.M. For example, the mean temperature for all the Januarys of the twelve years was 31.5° F. at 7 A.M.; 38.2° F. at 3 P.M.; and 34.2° F. at 11 P.M. Adding these together and dividing by three we have 34.6° F. as the average mean January temperature for the period.

The mean of the highest temperature for any given month is the average daily maximum temperature of all the days of that month throughout the entire period of observation. Thus, for example, in the period of thirteen years there are, for the month of January, $13 \times 31 = 403$ days, and 40.5° F. represents the maximum height which the thermometer may be expected to reach on each of these days. This temperature, therefore, represents the maximum temperature of a normal January day. In the same way the mean of the coldest is obtained; if we subtract one from the other we have the average daily variation or range of temperature. In this case, for instance, it is 13.5° F. for January. The highest or maximum temperature is the highest reached upon any day of the given month in any year of the period; for example, 71° F. was the highest temperature in any day of any January of the period. The lowest or minimum is the lowest reached on any day—*e.g.* 6° F. in this case. These extremes, as Dr. Richards remarks, represent the "chances" the invalid has got to take in any resort; they do not indicate what temperature he may expect, but what it may be his good or evil fortune to encounter.

The other terms used in the table are self-explanatory. EDWARD O. OTIS.

von Bamberger, Heinrich.—Born in Prague, Bohemia, Dec. 27, 1822. He received the degree of Doctor of Medicine, from the University of his native city, in 1847. In 1854 he was called to fill the Chair of Special Pathology and Therapeutics in the University of Würzburg. In 1872, upon the death of Oppolzer, he was made Professor of Special Pathology

and Therapeutics, and Director of the Medical Clinic, in the University of Vienna. His attractive manner of lecturing and the clear and logical explanations of disease which he made at the bedside soon rendered him one of the most notable members of the Faculty of Medicine. He died November 9, 1888.

Bamberger's two most important publications are these: "Lehrbuch der Krankheiten des Herzens," Vienna, 1857; and "Die Krankheiten des chylopoetischen Systems," 2nd edition, Würzburg, 1864.

A. H. B.

Bamboo Brier.—Under this name the tuberous roots of *Smilax pseudochina* L. (fam. *Liliaceæ*) are quite extensively used in the Southern States as a substitute for sarsaparilla, their near relative.

H. H. Rusby.

Bandaging.—Bandages are used for the following purposes: to apply firm pressure, to secure splints or dressings, to afford support, or to correct deformity. They are made of almost any fibrous material, as

Fig. 613.—Rolling a Bandage.

gauze, flannel, unbleached muslin, or cheese-cloth; but whatever the material, it must be both strong and supple. The most commonly used bandage is the "roller" bandage; and it is to this kind that the following remarks are applied. This is of various lengths and widths, according to the parts to which it is to be applied. Thus, for digits the roller should be three-quarters of an inch wide, and two or three yards long; for upper limb and head, two to two and a half inches wide and about six yards long; for lower limb, two and a half to three inches wide and about eight or nine yards long; for the trunk, four to six inches wide and about ten yards long. The material must be *torn* into strips and have neither selvage nor seams.

To make a "roller," turn about six or eight inches of bandage upon itself, and then roll this upon itself till it is a hard and firm cylinder; this forms a center around which as much more material as is necessary can be rolled. This rolling is accomplished by holding the two poles of the cylinder between the thumb and fingers of one hand, while the unrolled part passes between the thumb and index-finger of the other hand. The hand holding the roll is alternately supinated and pronated, the cylinder gradually getting larger (see Fig. 613). The center cannot be displaced from a properly rolled bandage. Bandages were formerly thus rolled by hand, but this wearying and tedious method is now replaced by some simple form of machinery.

The free end of the "roller" is called the *initial extremity;* the end in the center of the cylinder is called the *terminal extremity;* between these two extremities is the *body;* there are two surfaces, the *external* and *internal.*

When each extremity of the bandage is rolled toward the center, so that two cylinders are formed, the bandage is called a "double-roller." The ordinary single "roller" answers almost all purposes.

Bandaging cannot be learned from a book, but a few general rules may prove of service. The surgeon should face the patient and not stand at the side of the limb. The limb should be placed in the position it is to occupy when it is bandaged. The external surface of the roller is to be applied to the part; it should pass from the inner side, over the front, to the outer side, and from below upward. If the left limb is to be bandaged the surgeon should use his right hand and *vice versa;* hence the ambidextrous man has the advantage. Use a narrower bandage in preference to a wider one, except in bandaging the trunk. Bind firmly, evenly, and tightly, but not too tightly.

To remove a bandage, unwind the bandage a few turns and at the same time gather up the folds in a loose mass; rapidly transfer this gradually increasing mass from one hand to the other, taking care that the part does not become entangled in the loops. Bandage scissors may be used.

Bandages have been named from their use (as suspensory of breast), mode of application (as spiral, circular, reversed), shape (as figure-of-eight, spica), originator (as Barton, Gibson, Velpeau), etc.

Many names and varieties formerly used are now obsolete, as dolabra, ascia, etc.; and others are obsolescent. The modern tendency is toward simplicity; and bandaging is no longer the fine art it was once considered. The elaborate details formerly indulged in are not now considered necessary. But at the same time bandages should be applied properly, securely, and neatly. There is no excuse for the careless bandaging now seen more often than was formerly the case. For our present purpose bandages may be considered as:

1. *Simple,* including circular, oblique, spiral, spiral reversed, spica, figure-of-eight, recurrent.
2. *Compound,* including **T** (single and double), four-tailed, many-tailed, and handkerchief.

1. *Simple.*—(*a*) *Circular,* in which each turn exactly covers the previous turn. This is used for cylindrical parts of the body as the forehead, neck.

(*b*) *Oblique.* This is used to retain dressings loosely applied (as in burns); the succeeding turns do not overlap at all (see Fig. 614).

(*c*) *Spiral,* in which each turn overlaps about one-third of each previous turn. Used for conical parts of the body, but is now largely replaced by—

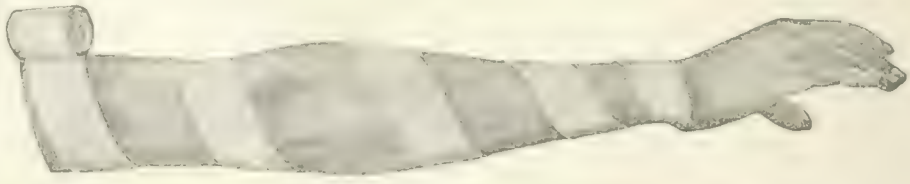

Fig. 614.—Oblique Bandage.

(*d*) *Spiral Reversed.* Since in the *spiral* the upper edge is tight, while the lower is loose, the spiral reversed was introduced to remedy this defect. To make a reverse, the bandage must be kept rolled up with three or four inches of slack only, and the bandage retained in place by finger and thumb; without traction turn the bandage down with a good slope down-

ward, so that it is well doubled over. Some little practice is necessary to get the knack of doing this

Fig. 615.—Spiral Reversed, I.

neatly and well. The commonest error is in holding too tightly what should be the "slack," and in not making sufficient slope. Figs. 615, 616, 617, and 618, show this bandage in progress and completed.

(*e*) *Figure-of-eight* looks on completion much like a spiral reversed, but its application is not the same (see Testudo and Spica). It is used over a joint or on the length of a limb, but care must be taken to have a

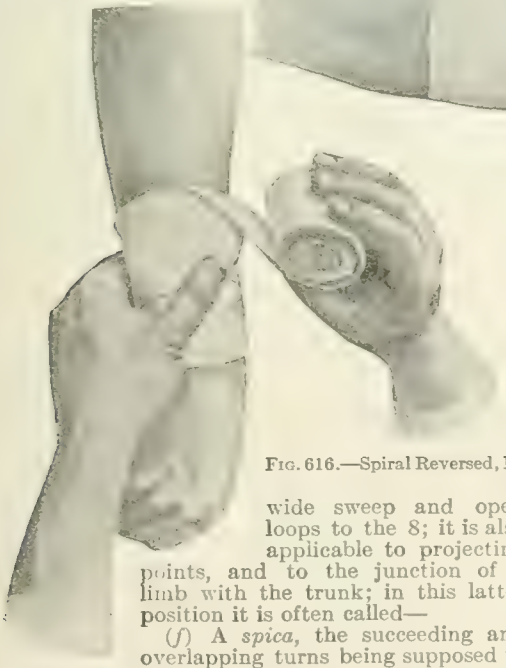

Fig. 616.—Spiral Reversed, II.

wide sweep and open loops to the 8; it is also applicable to projecting points, and to the junction of a limb with the trunk; in this latter position it is often called—

(*f*) A *spica*, the succeeding and overlapping turns being supposed to resemble an ear of corn (*spica*) There are many varieties of spica: ascending, descending, anterior, posterior, lateral, single, double. See Fig. 621.

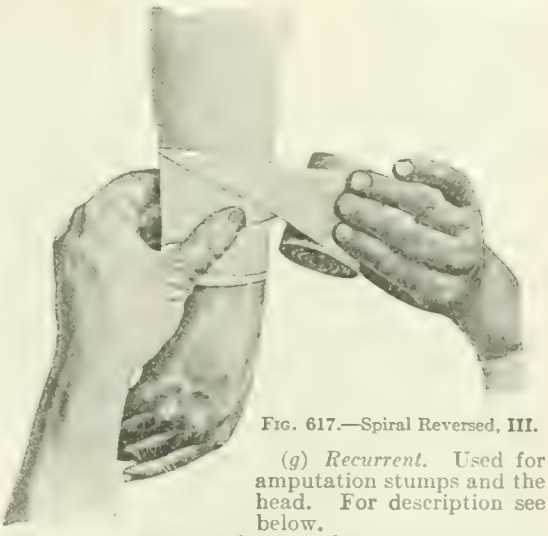

Fig. 617.—Spiral Reversed, III.

(*g*) *Recurrent.* Used for amputation stumps and the head. For description see below.

(*h*) *Testudo* is a modification of figure-of-eight used about an articulation. In the testudo *inversa* the spirals overlap from without inward, the last turns covering the center of the joint; while in the testudo *reversa* the first turn passes over the center of the joint, and the spirals diverge therefrom (see Figs. 619 and 620).

Head. *Recurrent Bandage.*—Take a roller and make two circular turns round forehead; then at center of forehead hold bandage, give it half a turn, take it over to occiput, have an assistant

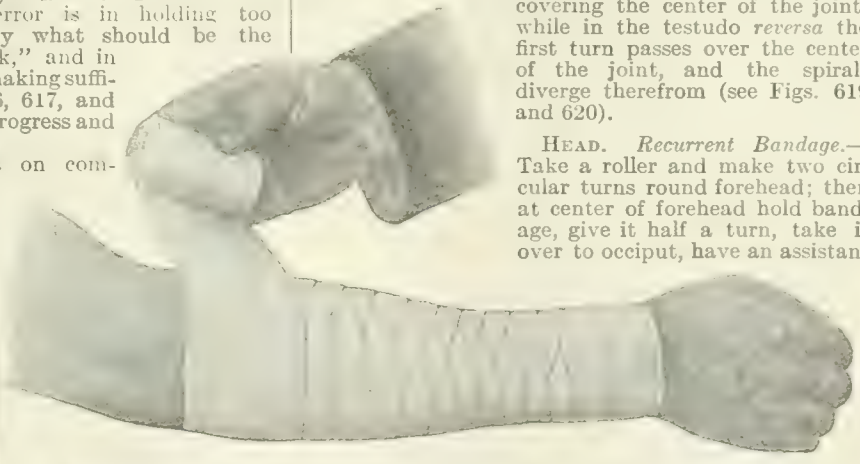

Fig. 618.—Spiral Reversed Completed.

hold it there, and then after half a turn go forward again to forehead, just overlapping a portion of the previous turn. Continue this until the scalp is covered all over, and finish with two circular turns round the

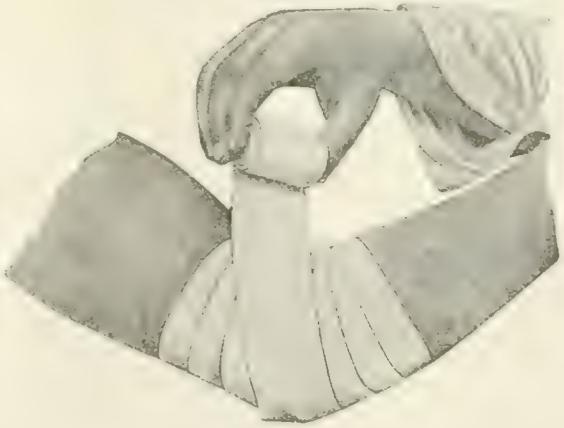

Fig. 619.—Testudo Inversa.

forehead; insert a few pins where the pieces overlap (see Fig. 622). A similar proceeding is used for an amputation stump.

A more secure bandage for the scalp is the *transverse recurrent;* in this, the roller is passed *transversely* over the head instead of backward and forward.

Fig. 620.—Testudo Reversa.

Barton's Bandage.—Begin at external occipital protuberance, go outward, upward over right parietal bone, across vertex, down left side of face in front of ear, under chin, and up the right side of the face in front of ear to vertex, then over left parietal bone to starting-point. Now take a turn round right side of jaw across chin, round left side of jaw, back to

Fig. 621.—Spica of the Shoulder.

Fig. 622.—Recurrent Bandage of the Head.

nucha, and up to occipital protuberance. Repeat from beginning and fasten at points of junction. This bandage is among the most useful of the bandages for the head, and is employed to fix the lower jaw in cases of fracture or dislocation of that bone, and also to apply dressings to the chin (Fig. 623).

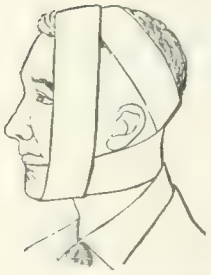

Fig. 623.—Barton's Bandage.

Fig. 624.—Galen's Bandage.

Somewhat similar, and used for the same purpose, is *Gibson's bandage.* Owing to its liability to slip and change its position, it is not so satisfactory as Barton's bandage.

Galen's bandage, sometimes called poor man's bandage, or six-tailed bandage, is very easily made and applied. Take a piece of cloth or handkerchief wide enough to reach from the occiput to the eyebrows and long enough to come down and meet under the chin. Each side is cut into three strips or tails, leaving a whole piece of from four to six inches on top of the scalp. Then putting the bandage in place take the two middle tails and fasten them under the chin, bring the two anterior tails backward and the

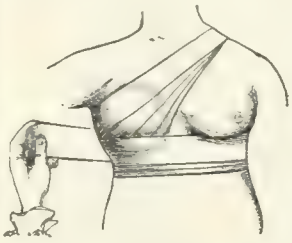

Fig. 625.—Breast Bandage.

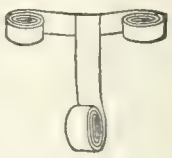

Fig. 626.—T-Bandage.

two posterior ones forward, and fasten them over the temporal region (see Fig. 624).

Four-tailed bandage (for scalp and fracture of lower jaw).—Fit the center snugly over the chin, take the two under tails and bring them up over the top of the head well forward, and tie them tightly there; then bring the upper tails and tie them tightly over the lambda. Finally, tie these two knots together. Considerable pressure can be obtained with this bandage.

For the Eye.—Place a narrow bandage over head and let it hang down in front of *sound eye;* then over this pass a circular bandage round both eyes. Fasten the posterior end of the narrow slip to the circular bandage, and lift the anterior end of the narrow slip and fasten it on itself, thus uncovering the sound eye (this is called Borsch's bandage).

Fig. 627.—Gauntlet of the Hand.

Trunk. *Spiral of Chest.*—One or two circular turns are taken around the waist, and the bandage is carried upward, with ascending spirals, each over-lapping one-half of the previous turn, as far as the axilla. The roller is now carried round to the back, then obliquely over the opposite shoulder, and down to the starting-point in front. Here it is pinned, also wherever the vertical piece crosses the horizontal turns.

Bandage of Breast.—Take the roller round the waist below the breast, commencing in front and passing

Fig. 628.—Velpeau's Bandage.

Fig. 629.—Desault's Bandage.

toward the sound side; then ascend over the lower part of the injured breast to the opposite shoulder, returning by the axilla to the horizontal turn where it passes round the waist again. The oblique turns over the breast are continued and carried up to the shoulder till the gland is entirely covered (see Fig. 625).

Another simple *bandage of breast,* equally effective

for compression and support, is made of a wide strip of cloth passed round front of chest over one or both breasts, under arms, and meeting at back, where by means of eyelets and lacing considerable pressure can be exerted.

T-bandages (Fig. 626) are made of two strips fastened to each other at right angles; this bandage is chiefly used in keeping dressings in the perineum. The transverse part is fastened round the body, and the tail or tails brought up between the thigh and genitals and fastened to the transverse part.

Upper Extremity.—Take two circular turns about the wrist, then go obliquely across the dorsum of the hand to the extremity of the fingers, then by spirals and reverses ascend the hand to the root of the thumb. A few figure-of-eight turns will cover the wrist; the

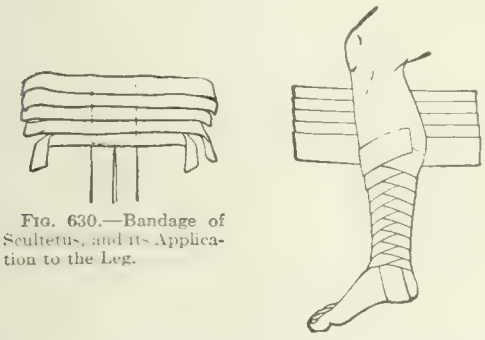

Fig. 630.—Bandage of Scultetus, and its Application to the Leg.

forearm is covered by spiral reverses, the elbow by a testudo or figure-of-eight, and the arm by spiral reversed turns.

For a *finger* or *fingers separately* use a roller of three-quarters of an inch thick, take two or three circular turns round the wrist, then go across the dorsum of the hand to the root of the finger, then take oblique turns to the tip of the finger; here take a circular turn and then by means of spiral reverses reach the base of the finger and finish by figure-of-eight turns between finger and wrist, and a couple of circular turns around wrist.

Gauntlet of the hand is represented in Fig. 627.

Velpeau's bandage for fractured clavicle, which was formerly much employed, is now seldom used, being replaced to a large extent by adhesive plaster. It is shown in Fig. 628.

Desault's bandage (Fig. 629), also much in vogue formerly, is now fast disappearing; it was cumbersome with its three rollers, axillary pad, and sling. The pad was either too small to be of much use, or else large enough to be injurious.

Spica of Shoulder.—Two circular turns and spiral reverses round upper arm from behind forward, go over the shoulder across front of the chest under opposite axilla and return across the back to the shoulder whence it started; repeat this five or six times. This is a figure-of-eight, the large loop going round the chest.

Lower Extremity.—Take two circular turns round ankle, and an oblique across dorsum of foot to the toes; make a circular turn here, and with spiral reverses cover the foot; take figure-of-eight round ankle, spiral reverse up leg; treat knee with figure-of-eight, and thigh with spiral reverses. If the heel is to be covered a testudo can be employed.

The bandage of *Scultetus* may at times be used advantageously for the leg. (See Fig. 630).

Spica of Groin.—Place a layer of cotton in the groin to prevent irritation. Begin with a couple of circular turns around the waist away from the hip to be bandaged, then down over the front of the thigh from without inward, then around back of thigh and up over the front of the groin and around waist. This plan is repeated, each turn overlapping one-third of previous turn; and finally a circular turn is taken round the waist.

Double spica of groin is more of a curiosity than of practical utility.

Fixed dressings, plaster-of-Paris bandages, and handkerchief dressings will be described in the article on *Dressings, Surgical.* R. J. E. Scott.

Bandl, Ludwig B.—Born in Himberg, Lower Austria, Nov. 1, 1842. He received the degree of Doctor of Medicine from the University of Vienna, in 1867. From 1875 to 1880 he held the position of an Instructor ("Privatdozent") in Obstetrics and Gynecology in the University of Vienna; and in the latter year he was made an extraordinary professor in the same branch of medicine. In 1878 he received the appointment of Director of the Section of Women's Diseases in the General Poliklinik of Vienna. In 1886, a very short time after he had been called to fill the regular Chair of Obstetrics and Gynecology in the University of Prague, his mind became affected, and he was sent to an asylum in Döbling, near Vienna. He died in the latter institution, from disease of the brain, on Aug. 26, 1892. Bandl's ring, the contraction ring marking the division between the upper and lower segments of the uterus, was named after him because it was he who first described it.

The following are among Bandl's more important published writings: "Ueber Ruptur der Gebärmutter und ihre Mechanik," Vienna, 1875; "Ueber das Verhalten des Collum uteri in der Schwangerschaft und während der Geburt," Stuttgart, 1878; and "Die Krankheiten der Tuben, des Beckenperitoneums und Beckenzellgewebes," in Pitha-Billroth's Handbuch der Chirurgie. A. H. B.

Banff Hot Springs.—Location.—Rocky Mountain Park, Canada.

Post-office.—Banff, Alberta.

Access.—From the east or west, viâ Canadian Pacific Railway.

According to the analysis of F. D. Adams, of the Geological Survey of Canada,

One Imperial Gallon Contains:

Solids.	Grains.
Chloride of sodium	0.771
Sulphide of sodium	0.624
Sulphide of potassium	0.673
Sulphide of magnesium	11.504
Sulphide of calcium	39.428
Bicarbonate of calcium	11.583
Bicarbonate of iron	0.126
Alumina	Undetermined.
Silica	2.789
Organic matter	Trace.
	70.498
Carbonic acid, free	3.041
	73.539

The waters also contain sulphureted hydrogen to the amount of 0.3 grain, equivalent to 0.8 cubic inch.

These well-known hot sulphur springs are situated on the line of the Canadian Pacific Railway near the eastern face of the Rocky Mountains. They are in an extensive reservation of 4,000 square miles in extent held by the Canadian Government as a national park. The waters are the property of the Government and are supplied to the sanitarium and the hotel. At the springs the waters are free to the public. The springs that are utilized are two in number, and issue from the mountain-side at about 800 and 1,000 feet above the Bow River, which flows through the valley, and 4,500 feet above sea level. The flow of water is continuous; that from the upper and hotter spring would form a cylindrical stream five inches in

diameter. The lower spring is much larger, and issues from a large cave in which is formed a natural basin some six feet in depth. The temperature of the water remains about the same all the year, that of the upper spring being 114° F. and that of the lower 95° F.

These springs are now among the most popular on the American continent and are visited annually by increasing numbers of tourists and invalids. Over 63,000 registered in 1911. The liberality of the Government in the case of the springs and the absence of extortionate charges making them a most desirable resort.

There has recently been erected a large modern sanatorium, under private management, for the convenience of invalids and such as desire the use of the waters apart from the surroundings of the large hotels. Every facility for the application of steam and hot water baths has been provided under the immediate supervision of the proprietor, who, with the aid of a staff of assistants, directs the proper use of the waters. There are a number of hotels in Banff, but the most popular is the Banff Springs Hotel under the management of the Canadian Pacific Railway. It provides accommodatiom for about 1,500 and an additional fire-proof wing is being erected. The water from the springs is conveyed by pipes to the Hotel and a complete modern equipment for hydropathic treatment is provided, with trained attendants.

The surrounding country is a series of snow-clad peaks, which possess all the grandeur of the mountain range, and a number of Swiss guides are kept to assist those who may desire to explore the mountains. Facilities for hunting and fishing are unsurpassed. The hotels and sanatorium are open throughout the year.

The following record is taken at the Government observatory on the spot:

BANFF, ALBERTA, N. W. T., LATITUDE N. 51° 10'. LONGITUDE W. 115° 35'. HEIGHT ABOVE SEA LEVEL, 1,542 FEET.

Months.	Pressure.			Temperature.			Rain, inches.	Snow, inches.	Precipitation, total.
	Monthly mean.	Extremes. Max.	Extremes. Min.	Mean.	Extremes. Max.	Extremes. Min.			
January...	25.22	25.61	24.96	16.4	30.2	−8.9			
February..	25.19	25.73	24.65	19.3	44.2	−23.2	...	24.65	2.47
March.	25.25	25.63	24.89	17.9	41.8	−27.3	.	9.95	0.99
April. ..	25.32	25.71	24.80	46.6	65.1	7.8	0.81	..	0.81
May.....	25.31	25.67	24.96	44.9	72.4	20.8	3.08	.	3.08
June ...	25.35	25.87	25.09	51.1	80.1	30.2	2.15	..	2.15
July ..	25.38	25.63	24.96	56.2	85.3	30.5	4.54	..	4.54
August....	25.39	25.59	25.12	59.9	85.2	32.0	2.37	.	2.37
September.	25.32	25.79	24.94	48.0	73.3	24.8	1.73	.	1.73
October...	25.39	25.79	24.89	35.0	47.6	15.8	1.09	.	1.09
November	25.20	25.63	24.76	20.9	41.8	−15.8	0.07	8.65	0.93
December..	25.36	25.85	24.76	19.2	48.0	−25.5	0.09	1.08	0.20
Year....	25.30	25.71	24.89	35.5	85.3	−27.3	15.93	44.33	20.36

NOTE.—Barometer not reduced to sea level

The air is exhilarating and the climate very favorable, the heat of summer and the cold of winter rarely being excessive. There are few places on this continent where the conditions for carrying out the high-altitude cure are as favorable as they are at Banff. The Canadian Alpine Club has erected its club house near the hotel.

BEAUMONT SMALL.

Bang's Method of Limiting Bovine Tuberculosis.—This resource is practically one of isolation of diseased animals in dairy herds, as a result of which badly infected stock is slowly but surely changed to sound stock without hardships to the dairyman or interference with breeding. Animals visibly diseased are promptly slaughtered and do not figure in the method. Isolation is carried out on all animals which react positively to tuberculin, and herds are tested annually. The reacting animals seldom present any evidence of ill health and are isolated in special stables or compartments, cared for by special attendants and used like sound stock for milking and breeding. The newly born calves are applied to the udders but one day, and are then isolated and fed on the boiled milk of healthy cows. The isolated calves are tested every six months with tuberculin and but few react positively. The isolation stables are thoroughly disinfected.

The method originated with Professor B. Bang of the Royal Veterinary School, Copenhagen, and its successful application is due to his activities. His first tests were made in 1892 and one year later upon his initiative, the first State Aid was granted. It was not until 1905 that the farmers by forming an association for carrying out the principles of the method became officially cooperative in the movement. During the interim some originally badly contaminated herds showed such a degree of improvement that one of them is now supplying the city of Copenhagen with special milk for babies. In general it may be stated that the stricter the isolation the sounder the herd. In the earlier years of the method its strictness was the cause of considerable laxity in its enforcement, but with its money value proven, the shortcomings are found to be due less to neglect than to the lack of means of some of the smaller farmers. The State supplies all the tuberculin without cost and aids in other ways. E. P.

Banti's Disease.—The term splenic anemia was first introduced into medicine by Griesinger in 1867, but the condition which it denoted had been recognized over a score of years earlier. But since anemia and splenomegaly may each exist in numerous forms the association of the two conditions in the same subject did not necessarily represent a clinical entity. In 1882, G. Banti, pathologist in Florence, collected all the scattered cases of the association from literature, and analyzed them along with some personal material. He was thereby enabled to establish the existence of a definite malady of which the essential lesion is primary splenomegaly which in turn gives rise to a special anemic blood picture. As distinguished from secondary splenomegaly, the most striking peculiarity of the idiopathic form is its amenability to radical surgical intervention. Banti's monograph on the disease which has since been associated with his name is entitled "Dell' anemia splenica" and was one of the publications of the Royal Institute (University) of Florence. See *Splenic Anemia* and *Splenomegaly*.

E. P.

Bantingism.—This empirical diet against corpulence would be described to-day as of a low calorie (1,100), high protein type (fifty per cent. animal food), the daily allowance amounting to but twenty-five ounces, with reduction of carbohydrates and fats to a minimum. The chief interest of the subject at present is historical, as the diet itself is quite unscientific, despite the fact that it did secure, with hardships and some risk, results which are much more readily and safely obtainable to-day by other means. The diet was carried out and popularized by a lay Englishman, William Banting, for whom it is named. It is hardly correct, however, to state that he invented it, for its provisions are said to occur in a work on diet by a French physician which appeared shortly before Banting's experiments upon himself; and he also admits that he received advice on the subject from

a Dr. Harvey. After he had failed to take off flesh by training, he carried out his diet with marked success, his weight having been reduced thereby from 202 to 156 pounds. His popular pamphlet on the subject ("Letters on Corpulence, addressed to the Public") first appeared in London in 1863 and went through several editions, the last of which, much amplified, was published in 1869.

For many years the word Bantingism was synonymous with the dietetic management of obesity, even when the regimen used differed materially from that originally prescribed; and the verb "to bant" acquired some vogue in this connection. Eventually Bantingism was supplanted by scientific dietetics. (See *Obesity*.) E. P.

Barbados.—This is the most easterly of the West Indian Islands, and is about a five or six days' journey from New York. The island is about twenty-one miles long by fourteen broad, and has a total area of 166 square miles—a little larger than the Isle of Wight. The population is 199,542, or over 1,180 to the square mile, one of the most densely populated areas of the world. The negroes outnumber the whites by nine to one.

The island seems very flat as one approaches it, but it rises in terraces to a ridge culminating in Mt. Hillaby, 1,105 feet above the sea level. The soil for the most part is composed of coral limestone, and is very fertile. There are no streams of any importance, and no natural harbor, only an open roadstead, Carlisle Bay.

Barbados is said to be the healthiest of all the West Indian Islands. The temperature, as a rule, varies from 75° F. to 86° F., rarely, even on the coldest days, falling below 65° F. For three-fourths of the year invigorating N. E. trade winds delightfully temper the tropical heat. "On the windward side, the climate is especially invigorating, and the island is much patronized by residents in neighboring colonies as a health resort. There are two seasons, the wet and the dry, the latter extending from December to the end of May. The annual rainfall varies from 50 to 70 inches, the average being 57.74 inches. The mean relative humidity is 72 per cent. The death rate is not more than 20 per thousand.

There is no system of drainage at Barbados outside of the garrison, but it is said (Hutchinson) that the porous nature of the land renders this unnecessary. The town and suburbs are supplied abundantly with pure drinking water. Residence in Bridgetown itself is not to be recommended to invalids, but one may safely select either Hastings or Fontabelle, in the suburbs, or Scotland, which is considered the healthiest residence portion of the island. Cases of typhoid fever are occasionally encountered, and yellow fever is sometimes brought from the other islands, but there is almost perfect immunity from smallpox, diphtheria, scarlet fever, measles, and other infectious diseases. "The records of the garrison there for the last twenty-five years show that it is the healthiest station at which troops are quartered anywhere in the world" (Moxly). The accommodations are good and reasonable. The Marine hotel at Hastings, two miles from town, is an attractive place, with good sea bathing and is conducted by an American.

The characteristics of the climate are those of an insular tropical climate, moist, bland, and equable, with only slight variations in the temperature. The northeast trade winds blow steadily during the day, and as a rule they are not unpleasantly strong. During the dry season from December to May, there are no rains or heavy dews. Although sunstroke is said to be rare, it is wise to follow the custom of the natives and carry a sun umbrella during the hottest hours of the day—from eleven to four.

Such a climate as this is manifestly unsuited for cases of pulmonary tuberculosis. "It is more than useless," says one who has had a large experience with this climate, "to send consumptives to these islands." There are various conditions and diseases, however, which are greatly benefited by a residence here; such are the various forms of nervous prostration, or mental fatigue, neurasthenia, chronic renal diseases, the various cardiac derangements or diseases, catarrhal and irritative affections of the throat, and laryngitis. Such a climate is also very suitable for old people or those possessing little vitality, and for weakly children. It may also be recommended to those who desire to avoid the risk of bronchitis or other acute respiratory affections so common in northern latitudes. "Tropical islands," says Hutchinson, "are bad places for rheumatism; the same constant moisture that plays so large a part in curing nervous difficulties produces and intensifies all forms of rheumatic affections."

Sea bathing is one of the features of this island, the temperature of the water being about 78° F. At Hastings there is a reef of coral which protects bathers from the sharks. From the experience of a personal trial the writer can heartily recommend Barbados as a delightful winter resort. Edward O. Otis.

Barcoo Rot.—See *Veldt Sore*.

Bard, Samuel.—Born in Philadelphia, April 1, 1742. His father, John Bard, was one of the most distinguished practitioners of his time, the friend and companion of Franklin. After receiving his academic education at King's College, New York, to which city his parents had moved in 1746, Samuel Bard was sent (Sept., 1761) to Edinburgh to fit himself for the profession of medicine. He received the degree of Doctor of Medicine in 1765. Upon his return to New York he at once entered upon the practice of his profession, in association with his father. It was about this time that he took an active part in the organization of a medical school in New York, in connection with King's College (afterward named Columbia College). According to the statement of the late Dr. James P. White, one of the biographers of Dr. Bard, this medical school "would appear to be the first regularly organized complete faculty for that purpose in America." Philadelphia's claim to priority in the establishment of the first medical school in this country rests upon the undisputed fact that, for two or three years previous to the date of inauguration of the King's College school, lectures on medical topics had been delivered in that city. It was also largely owing to the influence and active work of Dr. Bard that a spacious and well-organized hospital, afterward known as the "New York Hospital," was established in 1791 on a beautiful plot of ground facing the city's main thoroughfare. During the occupation of New York by the British troops Dr. Bard removed to New Jersey, but in 1784, after the cessation of hostilities, he again resumed his professional duties in that city. "While the General Government was sitting in New York President Washington had recourse to Dr. Bard's professional skill in his own case." (Stone.)

Fig. 631.—Samuel Bard.

In 1798, after forming a partnership with Dr. David Hosack, Dr. Bard retired to his country seat at Hyde Park, on the Hudson, and continued to live there during the remainder of his life. "In 1813, when a separation took place between Columbia College and its Medical School, upon the remodelling of the latter, Dr. Bard became the President of the College of Physicians and Surgeons. This honorable position he continued to hold during life." (Stone.) His death occurred May 24, 1821.

The only large work published by Dr. Bard is that entitled: "A Treatise on Obstetrics." A. H. B.

Barger's Springs.—See *Greenbrier Springs.*

Barium.—Salts of barium are of more interest to the physician from the point of view of toxicology than from that of therapeutics. Barium compounds are all poisonous, the soluble ones, of course, more actively so than the insoluble. Therapeutically, barium has been assumed to have a power over scrofulous conditions analogous to that of iodides or of mercurials, but no striking results have ever been demonstrated from its use. The *chloride* is the only barium salt of medicinal interest.

Barium chloride, $BaCl_2.2H_2O$, is not now official in the United States Pharmacopœia. It is a white, crystalline salt, occurring in rhombic tablets, permanent in the air. It dissolves freely in water and diluted alcohol, and has a bitter, disagreeable taste. It can be given medicinally in doses of from one-tenth to one-half grain (0.006 to 0.03) well diluted. In syphilis and scrofulous conditions twice this dosage has been employed.

Barium dioxide, BaO_2, was official in the U. S. P. 1890, being employed in the manufacture of the solution of hydrogen dioxide.

Toxicology of the Barium Salts.—Several of the soluble salts of barium, especially the nitrate, $Ba(NO_3)_2$, and the chloride, $BaCl_2$, are used largely in the chemical laboratory as tests for sulphuric acid. The compound, however, which is most familiar in commerce is the sulphate, $BaSO_4$, which is known as *barytes* or *heavy spar.* This is a heavy, white, opaque substance, much employed as a general adulterant on account of its weight, but especially for mixing with and adulterating paints. Its high degree of insolubility deprives it of any specific poisonous action, except possibly as a mechanical irritant.

The soluble barium compounds, especially those above mentioned, are irritant poisons. Cases of poisoning by them are, however, rare, and have been mostly the result of accident, the salt having been mistaken for one of the ordinary saline cathartics.

In the recorded cases of poisoning by barium salts the quantities taken have usually been rather large, varying from one hundred grains to half an ounce. But one dram of the chloride and also the same quantity of the carbonate has caused death. The symptoms—which do not arise immediately—are those of irritant poisoning, nausea, with sharp burning pains in the stomach, followed by vomiting and purging. Loss of muscular power has been noted in some of the cases, but most have exhibited convulsions toward the end. No characteristic brain symptoms are developed, but giddiness and headache have been observed.

Postmortem examination shows the usual appearances of irritant poisoning, inflammation of the mucous membrane of the stomach and bowels, and extravasation of blood.

Death has usually occurred in less than twenty hours, in some cases even in two hours; the average period is about twelve hours.

The antidote in poisoning by barium salts is any soluble sulphate, such as Epsom salt, Glauber's salt, or alum. These form at once the insoluble and inert barium sulphate, which can easily be removed from the stomach by the promotion of vomiting. Anodynes and stimulants will also be necessary.

There is no difficulty in recognizing a barium salt. Sulphuric acid or any soluble sulphate produces at once an opaque, white precipitate of barium sulphate, distinguished by its entire insolubility in water, in acids, or in alkalies. R. J. E. Scott.

Barium Springs.—Iredell County, North Carolina.

Post-office.—Barium Springs.

Access.—Viâ Southern Railroad to Barium Springs station, thence one-half mile to the springs. The location is five miles from Statesville and forty miles from Charlotte. There is now a Lodge at the springs.

This spring has been known since 1775. From the fact that cattle refused to drink from it the spring was formerly known as "Poison" spring. It is located on the top of a rocky knoll, about fifteen feet higher than a brook not over forty feet distant, and eight to ten feet higher than eight other springs around the base of the knoll and over one hundred feet distant. The spring has no visible outlet, yet the water remains at a constant level, never freezing and never stagnating. There are nine springs in the group.

According to an analysis by Professor Ledoux it contains seventeen grains per United States gallon of barium sulphate and chloride, phosphoric acid, and iron. Professor Chandler's analysis shows the presence also of a small quantity of sulphuric acid, lime salts, and magnesia. The water is used commercially, and is said to possess value in syphilis, eczema, indigestion, and ulceration of the stomach.

Barlow's Disease.—See *Scurvy.*

Barnes, Robert.—Born in Norwich, England, September 4, 1817. He studied medicine at University College, London, and St. George's Hospital, becoming a member of the Royal College of Surgeons in 1842. After a year of study in Paris he returned to London where he obtained an appointment as obstetric surgeon to the Western General Dispensary, at the same time lecturing at the Hunterian School of Medicine and doing editorial work for the *Lancet.* In 1848 he took the M. D. degree and in 1859 became a fellow of the Royal College of Physicians. This same year he was appointed assistant obstetric physician to the London Hospital, becoming obstetric physician in 1863. Two years later he exchanged this for a similar position at St. Thomas's Hospital, and ten years later became obstetric physician at St. George's Hospital where he remained for another ten years, receiving then an appointment as consulting obstetric physician. During his term at each of these three hospitals he lectured on midwifery at the associated medical school. Barnes was one of the founders of the London Obstetrical Society and was its president in 1865–6. But this society having placed its seal of disapproval upon the practice of operative gynecology by professed obstetricians, he withdrew in 1884 and founded the British Gynecological Society, of which he was the honorary president up to the year of his death, in which year the two societies were reunited to become one of the section of the Royal Medical Society. He died on May 12, 1907.

Barnes was a teacher and lecturer rather than a writer, yet during his long professional life of half a century he made a number of contributions to medical literature. Among these were: "Obstetrical Operations," 1870; "Medical and Surgical Diseases of Women," 1873; "Obstetric Medicine and Surgery," 1884; "Causes of Puerperal Fever," 1887. He also read thirty-two papers before the Obstetrical Society; these are printed in the Transactions. The name of

Barnes is associated with a bag for dilating the cervix, and also with one of the pelvic curves which he described. T. L. S.

de Barthez, Antoine Charles Ernest.—Born in Narbonne, France, in 1811. He received the degree of Doctor of Medicine in Paris, in 1839. He is chiefly known as the author, in conjunction with F. Rilliet, of a large treatise on diseases of children, a work which was very popular in its day, and which was crowned both by the Academy of Medicine and by the Academy of Sciences. This book, which was first published (3 vols.) in 1843, passed through three editions, the last one in 1884. Its title is: "Traité clinique et pratique des maladies des enfants." Barthez died on December 6, 1891. A. H. B.

Barthez, Paul Joseph.—Born in Montpellier, France, December 11, 1734. He received his degree of Doctor of Medicine in 1753 from the University of his native town. In 1754 he visited Paris and remained there one year. During this period he made friends among the more influential classes and through their aid he secured the position of a regular surgeon in the army; but he soon tired of this life, and in 1761 he offered himself as a candidate for the vacant chair of medicine in the University of Montpellier and was accepted by a unanimous vote. It was said of him, as Haller once said of Boerhaave, that "other physicians may be his equal in knowledge, but in the art of teaching he has not a single rival." His practice increased and brought him a fair share of wealth, but in the course of a few years he lost interest in his professional career in Montpellier and aspired to such higher honors as were obtainable only in a metropolitan city like Paris. Thus in 1781 we find him established in that city and already beginning to receive the consideration and respect which he so much coveted. The Duke of Orleans chose him as his first physician, in succession to Tronchin who had recently died. In the years which followed still other and greater honors were conferred upon him, but they failed to bring Barthez much genuine happiness or satisfaction. His bad temper made it extremely difficult for others to get along with him and also kept him in a constant state of dissatisfaction with himself. He therefore experienced much unhappiness in his old age. Death occurred from stone in the bladder on October 15, 1806. Of his published works it will be sufficient to mention the following two as being the most meritorious: "Nouveaux éléments de la science de l'homme," Paris, 1806, 2 vols.; "Nouvelle mécanique des mouvements de l'homme et des animaux," Carcasonne, 1798. A. H. B.

Fig. 632.—Paul Joseph Barthez.

Bartholin's Gland.—See *Vulvovaginal Gland.*

Bartholinus, Caspar or **Gaspard.**—The son of Thomas and grandson of the first Caspar, or Gaspard, Bartholinus was born in Copenhagen in 1655. In 1674, when but nineteen years old, he received from the king the honorary appointment of professor of philosophy at the University. For the next three years he studied physics and anatomy at various universities in Europe, and in 1677 began to lecture on these subjects in Copenhagen. In 1678 he received the degree of Doctor of Medicine. For nearly a quarter of a century he continued his studies in anatomy, lecturing regularly on this subject and on physics at the University, but in 1701 practically retired from professional work, having become greatly interested in politics. He died in 1738.

Caspar Bartholin described the duct, also called ductus major Rivini, and the gland (glandula vestibularis major) which are called by his name. The discovery of these structures is sometimes, however, erroneously credited to his father or his grandfather. T. L. S.

Bartholinus, Thomas.—Born in Copenhagen, Denmark, October 20, 1616. His medical studies were conducted at first under the guidance of his father, Kaspar Bartholinus, who was a man of considerable distinction as a physician, philologist, and theologian; but in 1637 Thomas went to Leyden, in Holland, for the purpose of perfecting his knowledge of the science of medicine. Afterward, in accordance with a custom which was almost universally observed at that period, he traveled over a large part of Europe, visiting first Paris or Montpellier, and remaining two years in one or the other of these centers of learning. Then he passed over into Italy and devoted three years to the study of anatomy, botany, and the practice of medicine, in Padua. His work here was so highly esteemed that he was made Prorector of the University of Padua on November 26, 1642. He visited, one after another, all the most distinguished physicians in Naples, Sicily, and Malta. The degree of Doctor of Medicine was conferred on him by the University of Basle, October 14, 1645. Soon after his return to Copenhagen, in 1646, he was given the chair of mathematics, and in 1648 the chair of anatomy was also assigned to him. In 1656 he was chosen Dean of the Faculty of Medicine. Six years later he asked to be relieved of his professional and executive functions on account of his physical infirmities. The King of Denmark granted his petition and conferred upon him the title of Honorary Professor. In 1670, when Bartholinus had the misfortune to lose his entire library through the burning of his château at Hagested, near Copenhagen, the King very generously granted him exemption from all taxes and assessments, made him his physician and one of his councilors, and at the same time bestowed upon him a large pension. Two years later the University gave him the position of librarian, thus restoring to him in large measure the privileges from which he had been deprived through the loss of his books. His death occurred on December 4, 1680. The ninety-two treatises which he is said to have written and published afford ample evidence that Bartholin was a man of great and varied erudition. A. H. B.

Bartlett Springs.—Lake County, California.

Post-office.—Bartlett Springs. Hotels and housekeeping cottages.

Access.—The Springs may be reached by one of two routes: Northwestern Pacific route, leaving Sausalito Ferry, San Francisco, at 7:45 A.M. train to Pieta, where automobile or stage may be taken to Clear Lake, thence by gas boat to Bartlett Landing where stage or automobile transports passengers to the Springs.

Southern Pacific route, Ferry foot of Market Street, 7 A.M., or Sacramento, 10:05 A.M.; thence to Williams, at which point automobile or stage may be taken to the Springs.

These springs have been known for upward of

forty years and have become widely noted as a health resort. No more pure and invigorating climate can be found than that of Lake County; and the Bartlett springs, being located in a cañon, with high mountains on the north and south, are particularly well located to resist sudden changes of temperature. The altitude is 2,350 feet. There is no rain from June to October. The thermometer shows a mean of 85° F. in the summer and is never below 20° F. in the winter; and the surrounding scenery is grand and inspiring. On the springs property, consisting of 1,800 acres, can be found hundreds of mineral springs, no two having exactly the same composition. The following analysis of the principal spring, by Mr. George E. Colby, shows an, alkaline-carbonated water of moderate strength which possesses, especially in the sodium, calcium, and magnesium compounds, active remedial agents.

One United States Gallon Contains:

Solids.	Grains.
Sodium chloride	0.50
Sodium bicarbonate	1.05
Potassium bicarbonate	.39
Magnesium carbonate	6.62
Calcium carbonate	30.14
Calcium phosphate	0.49
Calcium sulphate	.63
Iron compounds	Traces.
Silica	3.47
Lithium	Traces.
Borium carbonate	.05
Strontium	.00
Boric acid	Traces.
Organic matter	Traces.
Total	43.54

Gases.	Cubic inches.
Free carbonic acid	21.21
Ammonia	Faint trace.
Temperature of water	54° F.

Dr. Winslow Anderson's analysis shows slightly more solids per gallon and a somewhat smaller proportion of carbonic acid. There are other well-known springs here, including the "Soda," "Iron," "Sweet," and "Gas" springs. There are mineral tub and vapor baths with competent masseurs and attendants. A feature of great interest in the neighborhood is the gas tunnel, running eighty feet into the mountain-side. A large flow of carbonic acid gas issues steadily from the mouth of the tunnel. It rises to a height of eighteen feet above the ground and by force of gravity rolls down the mountain-side in considerable volume. Many small animals and reptiles, including birds, squirrels, lizards, etc., in trying to cross its path become asphyxiated. Skeletons of some of the victims may be seen for quite a distance from the tunnel's mouth. The waters of Bartlett Springs are highly recommended in chronic rheumatism, gout, sciatica, calculous diseases, diseases of the liver, scurvy, kidney disorders, eczema, dyspepsia, and chronic alcoholism. They are bottled and have an extensive sale on the Pacific coast.

Emma E. Walker.

von Basedow, Karl A.—Born in Dessau, Germany, on March 28, 1799. His medical studies were prosecuted chiefly in Halle, Prussian Saxony. He established himself in practice in Merseburg in 1822, and remained there until the day of his death, which occurred on April 11, 1854, from an infection contracted at a postmortem examination of the body of a person who had died of "spotted typhus." The work which has given Basedow a permanent place in the history of medicine, will be found in "Casper's Wochenschrift" for the year 1840. The article is entitled: "Exophthalmus durch Hypertrophie des Zellgewebes in der Augenhöhle." The disease here referred to is known at the present time as "Basedow's disease," "Graves' disease," or "exophthalmic goiter."

A. H. B.

Basedow's Disease.—See *Exophthalmic Goiter.*

Baseilhac, Jean.—This distinguished surgeon-monk, better known as Frère Cosme (or Côme) or Brother Cosmus was born in 1703 at Poyestruc, near Tarbes, in the department of Hautes Pyrénées, France. Both his father and his grandfather were masters in surgery, and he began in early youth to follow in their footsteps. He spent three years at Lyons, under the tutelage of his uncle, also named Baseilhac, and served for two years as a pupil in the Hôtel-Dieu, the great hospital of Lyons. From that city he went to Paris, and in 1726 was admitted as a pupil in the Hôtel-Dieu of that city, and not long afterward he was appointed surgeon-in-ordinary to Prince François-Armand of Lorraine. Upon the latter's elevation to the dignity of Bishop of Bayeux, in Normandy, young Baseilhac followed him to his new place of residence, and took charge of the hospital which he had built at his own expense. In 1729, after the death of the bishop, Baseilhac was received as a member of a religious brotherhood; and from that time onward he bore the name of "Brother John of St. Cosmus," or Frère Cosme. The taking of this step was apparently designed by Baseilhac as a means of enabling him to devote himself more completely to surgical work, for which he felt that he had a special vocation; and, as cases of stone in the bladder came under his care at that period in increasing numbers, he turned his attention more particularly to the cure of this condition by operative interference. In the main the results were surprisingly good, and the lateral operation and the concealed lithotome were soon adopted by the majority of French surgeons, and by many surgeons in other European countries. The constantly increasing number of the patients with stone in the bladder who required operative treatment led to the establishment in 1753, by Brother Cosmus, of a special hospital for such cases in the vicinity of the gate of St. Honoré in Paris. It is said that over one thousand lithotomies were performed in this institution, either by its chief or by his nephew, who acted as his assistant. Brother Cosmus died on July 8, 1781, at the age of seventy-eight.

According to Dezeimeris the art of surgery is indebted to Frère Côme for other improvements besides that which he introduced in connection with the operation of lithotomy. It appears that, from 1750 onward—that is, only a little later than Daviel—he performed the operation of extraction for cataract with instruments of his own invention. Before the time of Daviel, it will be remembered, couching was the only operative procedure employed for the relief of this condition. Brother Cosmus performed a large number of successful operations by the extraction method. Finally, Scarpa, in his treatise *Sul taglio ipogastrico per l'estrazione della pietra nella vescica orinaria* (Milan, 1820), speaks of his operation for the extraction of a stone from the bladder by the hypogastric route as practically a new method, and as reflecting everlasting credit upon its author.

Of the published writings of Baseilhac, the following deserve mention: "Recueil de pièces importantes sur l'opération de la taille faite par le lithotome caché, avec un mémoire concernant la rétention de l'urine causée par l'emabrras du canal de l'urètre," Paris, 1751; "Addition à la suite du recueil de toutes les pièces qui ont été publiées au sujet du lithotome caché," Paris, 1753; and "Nouvelle méthode d'extraire la pierre par-dessus le pubis," Paris, 1779.

It is a curious commentary on what makes for fame that Baseilhac's name, in religion has been preserved, not in relation to his surgical work, but attached to a caustic paste of arsenic, red sulphide of mercury, and burnt sponge, known as Frère Côme's paste.

A. H. B.

Basil.—(fam. *Labiatæ.*) *Ocimum basilicum* L., the common garden basil, is an annual Asiatic mint, cultivated in kitchen gardens in Europe and America, and of a mint-like and agreeable odor. The drug consists of the dried herb, which contains about one and a half per cent. of *essential oil,* consisting mostly of a stearoptene, basil camphor, which readily crystallizes in the oil upon standing in the cold.

The use of basil is culinary rather than medicinal; it has the carminative qualities of the family, and may be used for the same general purposes. Its chief use is as a flavor. Dose of an infusion, *ad libitum;* of the oil, ♏. iij. to viij. (0.2 to 0.5).

H. H. Rusby.

Basle Anatomical Nomenclature.—See *Anatomical Nomenclature.*

Basophilia.—This term denotes that property of tissues in virtue of which they stain deeply with basic, as distinct from acid, dyestuffs. In its most narrow technical sense it characterizes in this respect certain red blood-corpuscles, not necessarily pathologically altered. In theory all strongly basic coloring matters are implied, but as a matter of practice the stains used to demonstrate the presence or absence of basophilia are restricted to two—pure methylene blue and the mixture known as Giemsa.

Basophilic staining is eminently granular or punctate in character; or in other words the stained objects are minute granules scattered throughout the cell-body. Hence synonymous with basophilia are such terms as basophilic granulation, basophilic stippling, etc. The granules exhibit a wide range in respect of numbers, size, shape, and mode of grouping. Thus they may be few or many, spheroidal, rod-like, or angular, etc., and may be either uniformly disseminated or grouped in lines or zones.

The significance of basophilia is practically unknown. It is not necessarily pathological, for it is occasionally encountered in blood apparently normal. It is seen in certain stages of embryonal blood and also in bone-marrow. It may be produced sometimes by feeding normal subjects with hemoglobin and dietetic articles containing much blood ("blood puddings").

In pathological states basophilia is very frequently seen in the anemias but is also encountered freely in various morbid states in which anemia is absent. It may be said in general to accompany all the anemias, but in a very variable degree, so that it is no criterion of severity and has neither diagnostic nor prognostic significance. Even in those forms of anemia in which it occurs most constantly it may be unaccountably absent. In pernicious anemia it is much more sparingly present than in some of the benign forms. In the so-called Biermer's anemia and also in post-hemorrhagic anemia its presence is said to be entirely without significance. On the other hand, as might be expected from analogy, when there has been absorption of hemorrhagic exudates, basophilia may be strikingly in evidence. In chlorosis it is usually but feebly present, while in the anemia of saturnism it may be markedly in evidence, but never in such a manner as to furnish a criterion of the severity of the intoxication.

The significance of basophilia has been the occasion of much controversy, based in part on conflicting finds. Of two camps of polemists, one holds it to be a degenerative, the other a regenerative phenomenon. Much depends apparently on the question of its relatively constant occurrence in normal embryos. Naegeli, seeking to harmonize the opposing views, asserts positively that basophilia is present at some period of embryonal life, although absent in both the earlier and later stages. This fact with its occurrence in bone-marrow leads him to conclude that the phenomenon is one of attempted regeneration. He finds no evidence, to offset this, that basophilia is the result of a toxigenic degeneration.

Edward Preble.

Bassia Oil.—See *Palm Oil.*

Bath, England.—A town of 53,761 inhabitants, beautifully situated in the valley of the Avon, on the slopes of surrounding hills, one hundred and seven miles southwest from London. Bath has been a town of much reputation for its thermal springs ever since the days of the Roman occupation, and extensive Roman remains still exist there. Throughout English literature frequent mention is made of Bath, and it has had various vicissitudes of fortune; having been at one time one of the most fashionable watering places of England, and then degenerating into a quiet and somewhat neglected residential town for retired and invalided officials. Quite recently, however, the reputation of the place has again been rising. Owing to its sheltered position, being surrounded by hills, Bath affords an excellent winter residence, and a course of treatment can be taken at any season of the year; although May, September, and October are considered the best months.

The following meteorological data are taken from "Climates and Baths of Great Britain," 1895, to which the writer is indebted for the facts contained in this article:

Observations for 20 Years (1866-1885). (Fahrenheit Scale.)

Seasons.	Mean.	Highest.	Lowest.	Range.
Spring	48.4°	51.2°	45.8°	5.4°
Summer	60.3	63.5	58.1	5.4
Autumn	50.7	52.3	48.5	3.8
Winter	41.4	46.3	36.4	9.9

Thirteen out of twenty winters had a mean temperature above 40° F. The mean annual rainfall was 32+ inches. Autumn is the wettest, and spring the driest season. The thermal waters are derived from three springs: the Hot Bath, of 120° F.; the King's Bath, of 117° F.; and the Cross Bath, of 104° F. They are the hottest baths of any in Great Britain, those of Buxton coming next. The waters come under the head of "simple thermal," and the analysis, according to Mr. Attfield, is as follows:

One Imperial Gallon Contains:

Solids.	Grains.
Calcium carbonate	7.85
Calcium sulphate	94.11
Calcium nitrate	.56
Magnesium carbonate	.56
Magnesium chloride	15.24
Sodium chloride	15.19
Sodium sulphate	23.16
Potassium sulphate	6.70
Ammonium nitrate	1.06
Ferrous carbonate	1.22
Silica carbonate	2.71
Total	168.36

Traces of rubidium, lithium, and strontium.

	Dissolved gas per imp. pint.
Oxygen	0.74
Nitrogen	4.60

There are various establishments for the application of these waters: (1) The King's and Queen's Public and Private Baths adjoining the Grand Pump Room; and adjoining the King's Bath is the Roman Bath. (2) The Royal Private and Hot Baths. The hot bath here is an open one holding 7,570 gallons. (3) The New Royal Private and Swimming Baths attached to the Grand Pump Room Hotel. (4) The Cross Bath, a cheap public one. All these establishments belong to the corporation of Bath.

In connection with these baths provisions are made for giving the "massage douches" like those at Aix-les-Bains, reclining douche baths, Berthollet's local vapor baths, the "Scottish douche," sitz baths, and various sprays and pulverizations for nasal and faucial troubles. There is also the umbrella spray chamber wherein strong but thin streams of hot mineral water play upon a metallic dome and are pulverized. The room in consequence becomes filled with a sort of mist, and is used for patients suffering from chronic catarrh of the respiratory passages. There are also swimming baths of various temperatures.

Originally the general method of using the waters externally was by immersion in deep cisterns, the patient standing in them covered with water up to his neck. Covered in this fashion he could move about to promote flexibility of the joints. These immersion baths are still in vogue, the temperature varying from 98° to 104° F. There are other baths arranged for patients in a reclining instead of an erect position, and also arrangements whereby helpless patients can be lowered into the water, like the impotent man at the pool of Bethesda. A fountain in the Grand Pump Room supplies water for drinking, the amount usually drunk being from four ounces to half a pint twice a day.

"Special virtue is claimed for the Bath treatment in diseases which involve the articular structures (chronic rheumatism), and sufferers from such diseases constitute a very large proportion of the patients who seek relief at Bath." In gout and gouty affections the Bath treatment appears to be especially efficacious. In anemia, neuralgia, and many diseases of the skin it is of undoubted value. It is also used in various other maladies, as those of the digestive, respiratory, and nervous systems. It is contraindicated in all acute diseases with high temperature, in pulmonary affections, in tuberculous affections of the joints, and in heart disease.

The accommodations are abundant, varied, and good.

From a personal visit the writer can attest to the attractiveness of Bath as a place of temporary residence; its situation, as has been said, is beautiful, and the city itself, with its crescents and terraces, its abbey church and its fine Victoria Park, and all its interesting history, has much to divert one. There are also pleasant excursions in the neighborhood. EDWARD O. OTIS.

Bath Alum Springs.—Bath County, Virginia.

POST-OFFICE.—Bath Alum. Hotel and cottages.

ACCESS.—This resort is situated midway between Millboro on the main line and Hot Springs on the valley branch of the Chesapeake and Ohio Railroad, being ten miles from either point.

The location is at the base of Warm Springs Mountain in a rugged, broken section of country. The weather during the season from May to November is characteristically clear, bracing, and delightful, with few disagreeable days. The springs are six in number. We present the following analysis of Spring No. 2, which is fairly representative of the group, by Prof. W. H. Taylor:

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Sodium sulphate	1.15
Calcium sulphate	1.71
Lithium sulphate	Trace.
Magnesium sulphate	.46
Potassium sulphate	.34
Aluminum sulphate	29.99
Ammonium sulphate	Trace.
Manganese sulphate	.03
Iron persulphate	26.78
Sodium chloride	.11
Silica	1.95
Sulphuric acid	2.88
Total	65.38

Spring No. 1 contains 4.65 cubic inches of carbonic acid gas per United States gallon.

It will be seen that the waters are strongly aluminous and chalybeate with a fair proportion of free acid. They are astringent and tonic in their effects. Thus they have been found useful in chronic disorders and relaxed conditions of the mucous membranes, in skin diseases, and in general debility.

EMMA E. WALKER.

Baths.—See *Balneology and Hydrotherapy.*

Batteries, Electric.—See under *Electric.*

Battey, Robert.—Born in Richmond County, Georgia, on November 26, 1828. He studied medicine in Philadelphia—partly at the College of Pharmacy, partly at the University of Pennsylvania, and the rest of the time at Jefferson Medical College—and received the degree of Doctor of Medicine from the latter institution in 1857. His permanent home, except for the short period (1872–1875) during which he occupied the Chair of Obstetrics at Atlanta, in the same State, was at Rome, Georgia. During his residence at Atlanta he edited the *Atlanta Medical and Surgical Journal.* It was also during this same period (about 1872) that he published an account of the operation which bears his name—"Battey's operation" (removal of the normal ovaries to induce an artificial menopause for the cure of uterine fibroids and other conditions). He died November 8, 1895.

Dr. Battey was a frequent contributor to periodical medical literature, most of his writings dealing with the subject already mentioned, as well as with such topics as the following: the operative treatment of vesico-vaginal fistula; injections of water into the large intestine; incision of the perineum for the relief of chronic catarrh of the urinary bladder; the removal of a large fibrocystic tumor from the side of the neck in the neighborhood of the carotid artery; etc. During the Civil War he served as Surgeon in the Confederate Army. A. H. B.

Baudelocque, Jean Louis.—Born in Heilly, near Amiens, France, November 30, 1745. He obtained his medical education in Paris, and was successful in securing a first prize in competition with his fellow students at the Royal College of Surgery. Not long afterward, the professor of midwifery was taken ill and was obliged to give up his lectures. Thinking that the illness would not be of long duration, and having been struck with the cleverness and good sense of Baudelocque, who had been following his instruction, he requested him to lecture in his place until his health should be restored. The invitation was accepted, and Baudelocque performed the duties of the position in such a satisfactory manner that he decided thenceforth to devote himself entirely to midwifery. In the meantime the regular professor, Solayrès, died. As Baudelocque proved to be both an admirable instructor and a most skilful accoucheur, only a short time elapsed

before he attained a wide reputation and a very large practice. A few months before his death (May 2, 1810) he was selected to be the accoucheur of the empress, Marie Louise.

When Baudelocque appeared on the scene midwifery was practically a perfected branch of medical knowledge. The part which he played, therefore, was not that of a material contributor to midwifery's stock of facts, but rather that of one who clarifies and simplifies the knowledge already possessed by his contemporaries. His manual dexterity was very great and his powers of observation unusually keen. It is perhaps not quite correct to say that he made no material contributions to the knowledge of midwifery existing at that time; he certainly perfected the art of ascertaining the diameters of the pelvis on the living subject, and he determined with greater accuracy the relations of these to the diameters of the fetal head. Of the numerous monographs and larger treatises published by Baudelocque it will be sufficient to name the following two: "L'art des accouchemens," Paris, 1781; "An in partu propter angustiam pelvis impossibili, symphysis ossium pubis secanda?" Paris, 1776. A. H. B.

Fig. 633.—Jean Louis Baudelocque.

Bauhin, Caspar.—Born in Basel, Switzerland, January 17, 1560. He began the study of medicine in his native city, but, desiring greater privileges for acquiring knowledge than could be there obtained, he visited Padua, Italy, and availed himself of the instruction given by such celebrated teachers as Picoluomini, Fabricius of Aquapendente, Mercurialis, Capivaccio, and still others. He devoted his time chiefly to the study of anatomy and botany. From 1589 to 1614 he filled the chairs of anatomy and botany in the University of Basel, and in the latter year he succeeded Felix Plater in the positions of first physician of the city and professor of the practice of medicine, in the University. His death occurred December 5, 1624. The ileocecal valve (valvula coli) is sometimes called, after this antomist, the valve of Bauhin. Of his numerous writings the following deserve special mention: "De humani corporis partibus externus, etc.," Basel, 1588; "De ossium natura," Basel, 1604; "De compositione medicamentorum," Francfort, 1610. A. H. B.

Bayacuru.—The root of *Statice brasiliensis* Boiss. (fam. *Plumbaginaceæ*), a seashore plant of the southern Atlantic. Containing twelve and one-half per cent. of tannin, this is a valuable astringent. There is no good authority for its use in other directions. H. H. Rusby.

Bayberry.—*Candleberry. Wax Myrtle.* These names and various aboriginal and foreign equivalents are applied to various species of the peculiar genus *Myrica* (fam. *Myricaceæ*), but especially to the *M. cerifera* L., a very abundant, medium-sized shrub growing on and near the Atlantic coast of the United States. Its leaves are strongly and very pleasantly fragrant, and have been used for their aromatic stimulant properties. The bark contains a considerable percentage of tannin, as well as a small amount of the volatile oil, some resin, and an amaroid. It has been considerably used in gr. xxx. doses as an astringent and tonic and also locally for its astringent effects. The fruits are thickly coated with wax, so as to impart a conspicuous bluish-white color to them, and, through their abundance, to the entire plant when in the leafless state. This wax has been removed and has found its way more or less into commerce. H. H. Rusby.

Bay Leaves.—Under this name three distinct leaves have come to be known. One of them, the Cherry Laurel—*Prunus lauro-cerasus* L. (fam. *Rosaceæ*)—is to be regarded quite as a spurious article, with composition (yielding prussic acid) and properties quite distinct. These leaves are about six inches long, sharply serrate, have one or more pairs of depressed glands near the stem on the under side, yield the bitter-almond odor when macerated, and have the same taste. Both of the others properly bear the name, and they agree closely in composition and properties. The Royal Bay, or European laurel, is the leaf of *Laurus nobilis* L. (fam. *Lauraceæ*). It is usually less than four inches in length, oblong, acute at both ends, very thick, pale green, entire, but with the margin peculiarly crisped or wavy at right angles with the surface. It lacks the large basal glands of the last, as well as its bitter-almond odor and taste. This is the leaf usually used as bay in cooking. The third, our formerly official bay leaf, or wild clove leaf, is from *Pimenta acris* (Swz.) Wight, (fam. *Myrtaceæ*), and yields the oil a description of which follows. These leaves, about as long as the last, are twice as broad. They are of a dark green or brown color, somewhat glossy, rather thin, and have very numerous, fine, straight parallel secondary veins. H. H. Rusby.

Bay, Oil of.—Oleum Myrciæ. A volatile oil distilled from the leaves of *Pimenta acris* (Swz.) Wight, (fam. *Myrtaceæ*).

The oil is usually distilled in the West Indies, and imported into the United States in bottles, although of late an increasing quantity has been distilled from the dried leaves, imported here. The oil thus obtained is not quite so bright and fragrant as the best imported, but is much better than the common grades. Oil of bay is a brownish or dark brown liquid, of an aromatic, somewhat clove-like odor, a pungent, spicy taste, and a slightly acid reaction. Specific gravity about 0.975 to 0.990. It is a mixture of light hydrocarbons with *eugenol* (see *Cloves*).

Its medicinal qualities are those of the stimulating oils in general (allspice, cajuput, cloves, etc.), but it is employed only as a grateful perfume. Bay rum, which is the form in which it is generally used, was originally made by distilling with rum from the fresh leaves and branches. But this imported perfume is now generally substituted by a simple solution of the oil in cologne spirit or alcohol, flavored or not according to the taste of the manufacturer. As it is considerably used about the sick, a formula was furnished by the Pharmacopœia, as follows: "Spiritus Myrciæ, oil of myrcia, 16 parts; oil of orange peel, 1 part; oil of pimento, 1 part; alcohol, 1,220 parts; water, a sufficient quantity." H. H. Rusby.

Bayle, Gaspar Laurent.—Born, August 18, 1774, in Vernet, a small village in the mountains of Provence, France. He began the study of medicine at the University of Montpellier, and then (in 1798) became a pupil in the Paris School of Medicine. Shortly afterward he received the appointment of Assistant

in Anatomy. The degree of Doctor of Medicine was given to him in 1801. From the latter date to 1808 he was connected with La Charité Hospital, first as interne and later as one of the regular attending physicians. His death took place on May 11, 1816.

Bayle was universally admitted to be one of the most skilful practitioners of his day in Paris. His chief characteristics were: wonderful tact in his management of patients; promptness in making a diagnosis, which commonly turned out to be correct; and the possession of the power of predicting, in the cases in which recovery was not to be expected, the precise nature and extent of the lesions that would be found at the postmortem examination. All his published works, which treat of a variety of medical topics, indicate that Bayle possessed in a high degree all those qualities which go to make up an observer of the first rank. A. H. B.

Bazin, Antoine Pierre Ernest.—Born February 20, 1807, at Saint-Brice, France. Although the son and grandson of physicians, young Bazin at first showed no inclination to follow in their footsteps, but rather wished to study engineering. Yielding, however, to the entreaties and almost commands of his father, he took up the study of medicine for which he showed from the start a peculiar aptitude. He obtained his medical degree in 1834. In 1847 he was appointed physician to the Hôpital Saint-Louis and from that time devoted himself chiefly to the study of diseases of the skin, becoming, in point both of time and of renown, one of the first of French dermatologists. In 1853 he published his first important work on the nature and treatment of the tineas, in which he demonstrated that they were parasitic in causation, and differentiated the Achorion, Trichophyton, and Microsporon. From 1856 to 1860 he published numerous articles on the scrofulous, arthritic, and herpetic dermatoses, and later on the syphilides. In 1862 his lectures on the diseases of the skin caused by external irritants were published, and finally he devoted considerable time to the study of balneotherapy in its relation to the cure of constitutional disorders and of diseases of the skin. In 1872 he left the Hôpital Saint-Louis, after a continuous service of twenty-five years, and during the remaining years of his life contributed a large number of articles on dermatological subjects to the "Dictionnaire encyclopédique des sciences médicales." On December 14, 1878, he succumbed to an attack of pulmonary congestion.

Fig. 611. Antoine Pierre Ernest Bazin.

Bazin's contributions to medical literature were, as above noted, almost exclusively on dermatological subjects, although prior to his appointment to the Hôpital Saint-Louis he had written several articles on general disorders, one of his first theses sustaining the theory that many of the pulmonary affections were merely local manifestations of systemic disease. For many years, and even to-day by French writers, the term Bazin's disease was applied to erythema nodosum and also to buccal psoriasis. T. L. S.

B. B. Mineral Springs.—Pike County, Missouri. Post-office.—Bowling Green. Hotels, in Bowling Green.

Access.—Viâ Chicago and Alton or the Hannibal and St. Louis Railroad to Bowling Green. This health and pleasure resort is open the year round.

The springs are two in number. Their waters are widely sold in the Western States. The following analysis was made in 1910:

	Grains per Gallon.
Silica	.99
Oxides of iron and aluminum	.75
Calcium	28.73
Magnesium	44.78
Sodium	3.58
Potassium	1.3
Lithium	.03
Sulphuric anhydride	195.43
Chlorine	1.68
Carbon dioxide	8.47
Combined oxygen	42.08
Phosphoric anhydride	Trace
Undetermined matter	.37
	328.21

This is a very strong sulphated-saline water, with excellent purgative properties, containing, as it does, the sulphates of both magnesium and sodium. As a laxative it is recommended in wineglassful doses at bedtime, the stomach being empty. It is said to possess tonic effects when taken in wineglassful doses or less after each meal. It is beneficial in disorder of stomach, liver, and kidneys. Its action as a diuretic and uric acid solvent makes it valuable as an antirheumatic. When heated and used for bathing it is valuable in rheumatism.

Emma E. Walker.

Bdellium.—The bdelliums, for there are two varieties, are gum resins of the fankincense type, from at least two, probably several species of *Commiphora*. The East Indian bdellium is reputed to come from *Commiphora mukul* (Hook) Engl.; that of Africa from *C. africana* (Arn) Endl. (fam. *Burseraceæ*). The latter is the variety official in France; neither is so in any other country.

Bdellium resembles myrrh in appearance and qualities. It is in small yellowish or reddish-brown tears, or sometimes in larger masses; transparent, fragrant, brittle. It softens between the teeth, and crackles in the flame. The odor and taste resemble those of myrrh, but are weaker. It contains about sixty per cent. of *resin*, between thirty and forty of *gums*, mostly bassorin, and one or two of *volatile oil*.

Bdellium is a mild local stimulant like myrrh, of which it is almost an exact duplicate, though inferior. It is sometimes used as an adulterant of myrrh. It is now and then used in Europe in plasters.

H. H. Rusby.

Beale, Lionel Smith.—Born in London, England, in 1828. After he had completed his medical education (probably not before 1857) he was made Professor of the Principles and Practice of Medicine in King's College, and an Attending Physician in King's College Hospital, in London. His death occurred March 26, 1906. Of his numerous contributions to medical literature the following deserve to be mentioned: "Tables for the chemical and microscopical examination of urine in health and disease," 1856; "How to work with the microscope," 1861, 4th edition; "The microscope in its application to practical medicine," 1867, 3rd edition. A. H. B

Bearberry.—See *Uva Ursi*.

Beard, George Miller.—Born in Montville, Connecticut, on May 8, 1839. Four years after graduation from Yale College, in the class of 1862, he began the study of medicine at the College of Physicians and

Surgeons, New York. During the first year of his course in that institution he published (1866) an essay entitled: "Electricity as a Tonic." Nine years later he published, in association with Dr. A. D. Rockwell, a book which attained considerable popularity—viz., "Medical and Surgical Electricity," 1875. Of his other publications the following deserve special mention: "Hay Fever, or Summer Catarrh," 1876; and "American Nervousness, with its Causes and Consequences (nervous exhaustion, neurasthenia)," 1880. For many years neurasthenia was called "Beard's Disease." He died in New York on January 23, 1883. A. H. B.

Bearsfoot.—The root of *Polymnia Uvedalia* L., (fam. *Compositæ*), a very coarse perennial herb, common through most of the United States. The alterative properties claimed for it are of the most vague character, and we have no good authority for its use. H. H. Rusby.

Beaumont, William.—An American army surgeon who, in the early part of the nineteenth century, made a most valuable contribution to our knowledge of the action of the human gastric juice upon different kinds of food. He was born in Lebanon, Connecticut, in 1785. From 1812 to 1840 he was a surgeon in the United States Army, being stationed first at Fort Niagara, N. Y., then at Michillimackinac, Michigan,

Fig. 635.—William Beaumont.

and finally at Plattsburgh, on Lake Champlain, N. Y. He afterward took up his residence in St. Louis, Missouri, and died in that city on April 25, 1853.

The event which gave Beaumont the opportunity of making his celebrated experiments is set forth by him in full detail in an article which he published in No. VIII of the *American Medical Recorder*, 1825, and which bears the following title: "The Case of Alexis St. Martin, who was wounded in the Stomach by a Load of Duck-shot, with Experiences." The full report of his experiments with the gastric juice which he obtained from St. Martin's stomach by means of a glass tube passed through the fistulous opening, will be found in the book which he published in 1833, and which bears the title: "Experiments and Observations on the Gastric Juice and the Physiology of Digestion," Plattsburgh, N. Y., 1833. It is a remarkable fact, and one that reflects great credit upon the intelligence of Beaumont, that he should so fully have appreciated the value of the opportunity which the case of St. Martin thus unexpectedly placed within his reach. Nor is it any less remarkable that he, a man so imperfectly trained for work of this nature and so scantily equipped with apparatus, should have succeeded in carrying out successfully the experiments which he made—experiments which shed a flood of light upon the physiology of digestion, the knowledge of which was at that period very scanty. A. H. B.

Beaumont, William Rawlins.—Born in London, England, in 1803. After receiving a liberal education he prosecuted his medical studies at St. Bartholomew's Hospital, as testified by Abernethy, whose dressing pupil he was, and whose esteem he had won, as also that of Sir Astley Cooper, Lawrence, Herbert Mays, Marshall Hall, and others of renown in the medical profession. In Paris he studied, during a period of ten months, under Amussat, who perceived in him "un zèle et une aptitude rares." He obtained the license to practise surgery, and was admitted a Member of the Royal College of Surgeons, London, in December, 1826. In 1836 he was elected a Fellow of the Royal Medical and Chirurgical Society, London, and he served as Surgeon to the Islington Dispensary for some years prior to 1840. In 1841 he went to Canada and settled in Toronto, where, two years later, he was appointed to the Professorship of Surgery in the University of King's College (now the University of Toronto). In 1872 he was elected Professor of Surgery in the Medical Faculty of Trinity College, and afterward Professor Emeritus.

In 1836 he invented, and described before the Royal Medico-Chirurgical Society, an instrument for passing sutures in deep-seated parts (as in the operation for cleft palate), which was admired by Brunel, the great engineer, and was reputed by Tiemann, the surgical instrument maker of New York, to have been the origin of the Singer sewing machine. An account of the invention was published in various places—in the Transactions of the Medico-Chirurgical Society for 1836, in the *Medical Gazette* for the same year, and, finally, in *The Lancet*, of March 17, 1866. Beaumont also invented several other instruments. He died on October 12, 1875, at the age of seventy-two.

Of his published writings the following deserve to receive special mention: "On the Treatment of Fractures of the Leg and Forearm by Plaster of Paris," 1831; "On Polypi," 1838; "A Case of Large Cartilaginous Tumor of the Lower Jaw," 1850; "Clinical Lectures on Traumatic Carotid Aneurysm," in *The Lancet*, 1854; "The Several Forms of Lithotomy," *ibid.*, 1857; and "A Deeply Penetrating Wound Through the Orbit (five and one-half inches deep), followed by Recovery," *ibid.*, 1862. (From data kindly furnished by Dr. A. Primrose of Toronto.)

A. H. B.

Bebeeru Bark.—See *Bibiru Bark*.

Béclard, Jules.—Born in Paris, France, Dec. 17, 1818. His father, Pierre Augustin Béclard, was one of the most learned anatomists of the early part of the nineteenth century. Jules received the degree of Doctor of Medicine in 1842. In 1851 he issued a new and revised edition of his father's book, "Eléments d'anatomie générale"; and in 1855 he published a treatise on physiology, entitled: "Traité élémentaire de physiologie humaine, etc." A sixth edition of this work was printed in 1870. He also contributed many articles to the "Dictionnaire encyclopédique des sciences médicales." In 1872 he was elected to the Chair of Physiology in the Medical Faculty of Paris, and in 1881 he was made Dean of the Faculty. His death occurred on Feb. 9, 1887. A. H. B.

Becquerel Rays.—These are invisible rays which are emitted by the disintegration of atoms, the force involved being known as radioactivity. This force

is not resident in all matter, or at least is not known to be, but is limited to the salts of four metallic elements, to wit, radium, uranium, thorium, and actinium, our knowledge of the latter being speculative. Radioactive substances give off rays of three different kinds. The alpha rays so-called represent atoms of helium which carry a positive electric discharge and have a velocity of about 15,000 miles a second. They are heat rays and do not penetrate solid matter. The beta rays consist of free electrons, identical with the electrons of the cathode rays of the vacuum tube. They possess at times nearly the velocity of light and can penetrate solid matter. The nature of the third type or gamma rays is less obvious, but it is generally believed that they are immaterial, consisting simply of a wave motion imparted to the ether by the beta rays and closely allied to Röntgen rays. The beta and gamma rays are inseparable. The exercise of radioactivity by the radioactive elements causes a progressive disintegration of the latter, with the formation of so-called "transitional elements." The latter have received special designations, usually numerical, as Radium A, Thorium B, etc., but in some instances they have individual names. Thus Polonium, sometimes mentioned as an element, is the same as Radium G. For a consideration of the parent radioactive elements and their derivatives see *Radiography*. The most significant belief concerning these elements is that radium itself is only a derivative of uranium. This, of course, involves the conviction that all the so-called elements are derivatives, and that those of lower atomic weights are derived from heavier ones. The known radioactive elements are the heaviest known.

The Becquerel rays were discovered in 1896 by Professor Henri Becquerel while experimenting with fluorescent salts with reference to their ability to send rays through opaque substances. A photographic plate having been enveloped in dark paper various fluorescent substances were placed outside the latter in full daylight. First it was found that a uranium salt was able to affect the plate, not only in the presence of daylight but even in darkness. Next it appeared that the new form of activity had no connection with fluorescence or it occurred with non-fluorescent uranium salts. Among those who took up the study of the new rays was Mme. Curie, a student who saw in them a good subject for her graduation thesis.

We have seen that of the Becquerel rays the beta and gamma rays were practically known before his discovery; for the former are very closely allied to the cathode rays and the latter to the Röntgen rays. Both are considered more fully under *Radiography*. The alpha rays, therefore, constitute the principle element in Becquerel's discovery. Many facts have been ascertained concerning them. They represent the greater part of the energy set free. Their properties are due largely to the fact that they are particulate, the particles being of considerable magnitude. Since their penetrative powers are slight their impact against various solid substances causes a notable series of phenomena. Many salts and crude minerals are rendered fluorescent, and this property is utilized for measurements of the rays. The latter can be deflected by the magnet and this property is likewise used for quantitative estimations. It was held originally that radioactive matter could render indifferent substances radioactive in turn; but later it was learned that radium emanations are merely deposited on the surfaces of bodies which arrest them. EDWARD PREBLE.

Bedbugs.—True bugs of the genus *Cimex*. Characteristic species suck blood from man (*C. lectularius*), and other vertebrates. Some species are also known to carry sporozoan diseases. See *Insects, parasitic*. A. S. P.

Beddoes, Thomas.—Born at Shiffnall, in Shropshire, England, on April 13, 1760. He received the degree of Doctor of Medicine from the University of Oxford in 1786, and two years later, after he had visited Paris, he was appointed reader in chemistry in the same institution. About the year 1792 he made preparations for establishing what he termed a "Pneumatic Institution," a place where various diseases might be treated by the inhalation of different gases. Six years later this institution was established at Clifton, with Humphry Davy as its first superintendent; but it seems not to have been a success, and was soon converted into an ordinary hospital for the sick. Beddoes died on December 24, 1808.

Of the different works which he published, the following deserve to be mentioned: "An Essay on Consumption," 1799; "An Essay on Fever," 1807; and "Hygeia, or Essays Moral and Medical," 1807. Beddoes is spoken of by his biographer in the *Encyclopædia Britannica* as "a man of great powers and wide acquirements, which he directed to noble and philanthropic purposes." A. H. B.

Bedford, Gunning S.—Born in Baltimore, Maryland, in 1806. After he had received the degree of Doctor of Medicine he visited Europe and remained there for two years, for further professional studies. Upon his return to this country in 1833 he was elected Professor in the Charleston (S. C.) Medical College. Then later (1834), in association with Dr. Valentine Mott, he founded in New York, the University Medical College—an institution in which he occupied the Chair of Obstetrics and Gynecology up to the year 1862. His death, from cerebral apoplexy, occurred on September 5, 1870.

Bedford's most important contributions to medical literature are his "Clinical Lectures on the Diseases of Women and Children" (eight editions up to 1868) and his "The Principles and Practice of Obstetrics" (four editions). A. H. B.

Bedford Springs.—Bedford County, Pennsylvania.

POST-OFFICE.—Bedford. Hotel.

ACCESS.—The Baltimore and Ohio and Western Maryland Railroads transfer passengers at Cumberland, Md., and the Pennsylvania Railroad at Altoona and Huntingdon, Pa.

The Bedford Mineral Springs have their source in a beautiful valley on the eastern slope of the Alleghany Mountains, at an elevation of ten hundred and eighty feet above tide water. The location is one mile and a half south of the old historic town of Bedford, the county seat of Bedford County, in a region noted for its pure, invigorating air, salubrious climate, and beautiful and varied scenery. The medicinal virtues of the springs were known as early as the year 1804.

Since those early days the resort has maintained a steady popularity with the tourist, pleasure-seeker, and invalid, and it may to-day be ranked among the best of the many excellent summer watering places which the country affords. In addition to the numerous attractions of climate, and scenery, the visitor will find a very comfortable modern hotel, well equipped with the most recent improvements. A good orchestra is maintained during the season. The magnesia spring has been mainly instrumental in giving the place its reputation. It issues from an opening in the rock, about three feet in length and eighteen inches in width, and flows about 2,000 gallons of water per hour, without interruption or intermission, the year round. A recent examination of the hitherto somewhat neglected Bowling Alley Spring shows it to be quite as strong in magnesium.

salts, while carrying less lime. We present analyses of these two springs, made in 1895 by Victor G. Bloede, analytical chemist, of Baltimore:

MAGNESIA SPRING.

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Sodium carbonate	2.04
Sodium chloride	.72
Magnesium sulphate	32.54
Magnesium carbonate	6.06
Potassium carbonate	.38
Calcium sulphate	107.80
Lithium chloride	.22
Silica	.36
Iron oxide	.05
Alumina	.11
Ammonia	.02
Total	150.30
Free carbonic acid	1.85
Water of crystallization and volatile matter	36.41

BOWLING ALLEY SPRING.

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Sodium bicarbonate	9.70
Sodium chloride	1.12
Magnesium sulphate	32.96
Magnesium carbonate	5.23
Calcium sulphate	83.20
Silica	1.10
Iron oxide	.04
Alumina	.09
Ammonia	Trace.
Total	133.44
Free carbonic acid	2.17
Water of crystallization and volatile matter	37.74

These analyses show very potent waters of the sulphated-saline and calcic variety. They are laxative in small doses, purgative in larger. Furthermore, they have a considerable diuretic influence, and each contains sufficient iron to counteract the debilitating tendencies often met with in waters of this character. The Magnesia Spring contains also a small amount of the chloride of lithium, which serves to widen the sphere of its probable utility. The Bowling Alley Spring is quite freely charged with that ever-valuable ingredient of saline waters, the carbonate of sodium, which renders it very useful as an antacid and antifermentative, in addition to its cathartic properties. These waters may be counted upon to render good service in flatulent dyspepsia, functional disturbances of the liver, abdominal engorgement, and chronic constipation. They are also highly recommended by many well-known physicians for gouty and rheumatic disorders and for affections of the kidney and bladder. They are used commercially. There are several other valuable springs in the neighborhood. The following is the analysis of one of these:

BEDFORD CHALYBEATE SPRING.

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Calcium carbonate	8.85
Magnesium carbonate	1.20
Iron carbonate	.44
Magnesium carbonate	Trace.
Sodium carbonate	.39
Potassium carbonate	.13
Calcium sulphate	2.74
Calcium phosphate	.03
Sodium chloride	.12
Hydrogen sulphide	Trace.
Silicic acid	.79
Carbonic acid (free)	5.60
Total	20.29

The physiological action of this water tends to increase the appetite, promote the digestion of food, and improve the quality of the blood. The predominance of the calcareous salts would seem to give the water an astringent and constipating influence. These effects, however, have not been observed by those who have used it freely. It has, in fact, seemed to exert a mild laxative action, and is furthermore quite an efficient diuretic. Its action resembles that of the well-known Bocklet Springs, near Kissingen, in Bavaria. The water is used for bathing as well as for drinking. The water is useful in cases of anemia, general debility, and amenorrhea, and in convalescence from acute diseases. This water and the residual salts obtained by evaporation are used commercially; an extract and an ointment are prepared from the latter

EMMA E. WALKER.

Bed-sores.—See *Decubitus*.

Beggiatoa.—The solitary genus of the family *Beggiatoaceæ* of the fission-fungi. The cells are of the form described under *Beggiatoaceæ* and contain sulphur granules; for this reason they are sometimes regarded as forming a sub-genus or species of *Thiothrix*.

T. L. S.

Beggiatoaceæ.—A family of Schizomycetes, or fission-fungi, comprising cells arranged in elongated filaments, not surrounded with a sheath, but provided with an undulating membrane. Division occurs in one (the transverse) plane only. The family includes but one known genus, *Beggiatoa*.

T. L. S.

Belascaris.—A genus of parasitic round worms in which the anterior end of the body is bent ventrally. *B. mystax* is often present in cats and has sometimes been found in man. See *Nematoda*. A. S. P.

Belknap Hot Medical Springs.—Lane County, Oregon.

POST-OFFICE.—Belknap Springs. Camping grounds.

ACCESS.—Viâ Southern Pacific Railroad to Eugene, 125 miles south of Portland; thence there is a good wagon road, and stages in summer go within 6 miles of the place.

The location of these springs is in the heart of the Cascade Mountains, 2,000 feet above the sea level. This is a very fine and picturesque region, and it presents many attractions to the tourist and invalid. The climate is equable, the weather during the summer months being generally clear and pleasant, with cooling winds.

The average summer temperature is 65° F., while it is stated that the average winter range is but twenty degrees lower. The Mackenzie River, near by, is famous for its magnificent trout; and deer and other game abound in this region. There is only one spring, but it yields about 12,500 gallons per hour. The temperature of the water is 138° F. The following analysis was made in 1894 by Prof. G. W. Shaw, of the Oregon State Agricultural College, at Corvallis:

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Calcium phosphate	13.91
Calcium chloride	62.20
Potassium chloride	7.68
Magnesium chloride	2.90
Sodium chloride	53.93
Manganese chloride	Traces.
Silica	4.72
Iron and alumina	.17
Total	145.51

The bathing facilities comprise medicated, steam, electric, and shower baths, hot or cold, with massage. A large swimming tank is an attractive feature. The baths are attracting considerable attention in the treatment of rheumatism, kidney disorders, syphilis, and skin diseases. EMMA E. WALKER.

Bell, Sir Charles.—Born at Edinburgh, Scotland, in November, 1774. After he had passed through the usual course of preliminary schooling he embraced the profession of medicine and devoted himself chiefly to the study of anatomy, under the direction of his elder brother, John Bell, the anatomist. While he was still a pupil, he published in Edinburgh, in 1798, his first work, entitled "A System of Dissections, explaining the Anatomy of the Human Body, the Manner of Displaying the Parts, and their Varieties in Disease." For many years this book was considered an excellent guide for the student in anatomy. In 1802 he published a series of engravings of original drawings, showing the anatomy of the brain and nervous system. In 1804 he wrote the third volume of "The Anatomy of the Human Body, by John and Charles Bell;" this volume containing the anatomy of the nervous system and of the organs of special sense. Toward the end of the same year he left Edinburgh and settled in London; but before leaving Edinburgh he had written his work on the "Anatomy of Expression." This book, which was published in London shortly after his arrival in that city, attracted a good deal of attention. Seven years later, in 1811, he published his "New Idea of the Anatomy of the Brain," in which he announced the discovery of the different functions of the nerves corresponding with their relations to different parts of that organ. In his larger work, "The Nervous System of the Human Body," published in 1830, the results of his long-continued and valuable researches in this comparatively new department of anatomy and physiology are set forth in more perfect detail.

FIG. 636.—Sir Charles Bell.

Charles Bell's reputation as a surgeon began in 1807, when he wrote a "System of Comparative Surgery," in which surgery is regarded almost wholly from an anatomical and operative point of view. This book at once placed him in the highest rank of English writers on surgery. In 1812 he was appointed surgeon to the Middlesex Hospital, and he retained this post for twenty-four years. During this period he published a number of treatises and articles on surgical topics; but it was not until 1839 or 1840 that he wrote his larger work, entitled "Institutes of Surgery." In 1830, when William IV. ascended the throne, Charles Bell was knighted. In 1836 he gave up his large practice in London and accepted the chair of surgery in the University of Edinburgh. His death occurred on April 28, 1842. Bell's paralysis and a number of other neurological eponyms were called after him.

Sir Charles Bell's remarkable skill as an artist undoubtedly aided him very materially in attaining his great reputation as an anatomist, as a physiologist, and as a surgeon; a reputation which appears to have been as great on the continent of Europe as throughout Great Britain and her colonies. A. H. B.

Bell, John.—Born at Edinburgh, Scotland, on May 12, 1763. He received his medical education at the University of Edinburgh, and in 1790 he began to give courses in anatomy, which attracted large audiences, and in which he was assisted by his younger brother Charles. In 1793 he published a book entitled "Discourses on the Nature and Cure of Wounds," and in 1801 his "Principles of Surgery." Bell's muscle, a band of muscular fibers, bounding the trigonum vesicæ, was first described by him. He died at Rome on April 15, 1820. (Consult also the preceding article on Charles Bell.)

A. H. B.

Bell's Palsy.—See *Facial Paralysis*.

Belladonna.—*Deadly Nightshade. "Black Cherry."* (For a description of the belladonna plant, see article on *Poisonous Plants*.) The belladonna plant yields two official medicinal articles, namely, *Belladonnæ Folia*, "the dried leaves," and *Belladonnæ Radix*, "the dried root of *Atropa belladonna* L. (fam. *Solanaceæ*)." The leaves are required to contain at least 0.3 per cent. and the root at least 0.45 per cent. of mydriatic alkaloids.

Belladonna is a native of Europe and adjacent Asia, where the drug is mostly collected from wild plants. In Europe it is also largely cultivated for medicinal purposes. It has become naturalized to a slight extent in the United States. The composition of leaf and root is very similar, the difference being rather in the greater quantitative irregularity of the leaves than in kind. The leaves do, however, contain a rank-smelling principle not present in the root, rendering them objectionable for some purposes, but possibly of greater therapeutic value. They contain also considerable chlorophyll, which causes their extract to impart an objectionable green stain to clothing, when used in plasters. Both articles may be regarded as exceptionally irregular and uncertain in quality. Some of the causes of this irregularity are not known, so that no methods of physical examination of the drug can eliminate them, a chemical assay being requisite. Others are known and can be detected by careful examination. Since the publication of the preceding edition of this work, the writer has given constant and careful attention to the character of importations of these leaves and roots, and has found both subject to frequent and serious adulteration with other leaves and roots. The most common adulterant of the leaves is *Scopola* leaf. This is much thinner and shows, in the mass, as blackish-brown and much more shrivelled. On soaking, and flattening, its shape is seen to be broadest above the middle, the base gradually tapering downward. Its fruit is a small pod, from which the upper part separates as a lid. Next in frequency and importance is the adulterant *Phytolacca* or poke-berry leaf. This is extremely difficult to detect except when the stem-tips, bearing the inflorescence, are present. These are slender racemes, from two to six inches long, bearing numerous buds as large as a pin-head, and perhaps some open flowers one-eighth to one-fourth inch broad. The leaves are thicker, stiffer, and nearly oblong. Those of henbane, digitalis, and verbascum are all hairy, while belladonna is smooth; those of henbane and potato are toothed or lobed, while the margin of belladonna is entire. The leaves of datura, or stramonium, come in a crumpled mass, closely resembling that of belladonna leaf, and one is often mistaken, upon superficial examination, for the other. The belladonna mass is, however, almost invariably of a brownish-green color, a bright green indicating an immature leaf, while that of stramonium is of a clear, usually a dark, green color. Upon soaking and flattening out a leaf, the large, angular teeth or lobes of the latter, with their very unequal base, contrast strongy with the entire margin, regular outline,

and nearly equal base of the former. As to the roots, they are greatly subject to substitution, adulteration, and imperfection of quality, which are much more readily detected by physical inspection than is the case with the leaves. Scopola is very largely substituted for belladonna, especially in Europe. Its constituents and properties are very similar to those of belladonna, but it contains some hyoscine. As the two drugs present not the slightest similarity, this action can be regarded only as wilful and deliberate, as is the addition of the roots of poke, burdock, medicago, and of one which appears to be wild, unpeeled marshmallow. The two last named are flexible, while belladonna is stiff and brittle. Burdock has a soft pith or a hollow center. The three last-mentioned forms of adulteration are highly objectionable, as the articles have no properties at all like those of belladonna. Poke-root is the commonest and most serious adulterant of all. A few years since not a pound of belladonna root was to be found in the American market that did not contain this dangerous adulterant and the federal authorities were obliged to permit the picking over of importations in order to provide the country with supplies. The detection of poke-root is not difficult. Its outer surface bears circular rows of very small, mostly lighter colored, wart-like projections. The transverse section of poke-root shows concentric rings of light and darker tissue, the one projecting slightly beyond the other. On longitudinal section these two tissues show as longitudinal bands. Dust scraped from the section shows needle-shaped crystals of calcium oxalate when viewed under the microscope, and the same is true of the leafy tops when mixed with belladonna leaves. The imperfection of genuine belladonna root, aside from obviously bad conditions of mould and worminess, relate to its being too young (when less than two-fifths inch in thickness) or old, thick, and woody. The active constituent resides chiefly in the bark; hence old thick pieces, in which the increase of weight is chiefly of inert woody fiber, must be inferior. The two drugs are described as follows:

The Leaves.—From ten to fifteen centimeters (four to six inches) long and about half as broad, ovate, abruptly and almost equally narrowed into a petiole of extremely variable length, the apex acute or acutish, but not acuminate or tapering, entire on the margin, smooth, thin, drying brownish green, the upper surface browner, the lower greener and paler, both surfaces minutely whitish punctate; odor slight; taste bitterish, somewhat acrid.

The Root.—In cylindrical, but slightly tapering, coarsely wrinkled pieces, bearing their bark, rarely exceeding fifteen centimeters (six inches) in length, having a thickness of ten millimeters (two-fifths inch) to twenty-five millimeters (one inch), often split; externally of a light brownish gray, much subject to abrasion, which reveals a lighter inner layer, internally whitish; breaking with the characteristic emission of a puff of dust, and exhibiting a nearly smooth and starchy fracture, indistinctly many-radiate near the bark; nearly inodorous; taste sweetish, afterward bitterish and strongly acrid. Portions of the stem and of thick, hard, woody crowns should not be included.

Composition.—The minor constituents of the leaves are starch, gum, wax, and asparagin; and of the roots, starch. The active constituents of both are the mydriatic alkaloids, about one-tenth to one-half per cent. in the leaves, one-fourth to three-fourths per cent. in the root. As regards the identity and precise relative amounts of the different alkaloids, discussion is in the present state of our knowledge unprofitable, and in view of their very similar therapeutic effects, equally unimportant. *Belladonnine* and *hyoscine* (if the latter be really present at all—see *Hyoscyamus*) are in such small amounts as to be absolutely unimportant. The only alkaloid other than *atropine* which is present in appreciable amount is *hyoscyamine*, and the action of this is so nearly identical with that of atropine as to render its presence of no importance. Theoretically, the relations of the two last named are of great interest. They are so closely similar that, even when in the pure condition, it is almost impossible to distinguish them. It is believed that very young roots will yield only hyoscyamine, old ones chiefly atropine. It is not by any means certain, however, that the extraction of one proves that it so existed in the living plant. It is, further, very uncertain as to the maintenance of their identity when the respective alkaloids are taken into the stomach or the system. Certainly their practical effects are generally regarded as identical, so that therapeutic interest in the drug centers finally in its percentage of total alkaloid. Since, according to the above showing, the preparations of belladonna must vary so widely, and as the determination of their strength is no longer difficult, none should ever be used whose percentage of total alkaloids is not known. The cultivated leaves of California, where this industry has been developed by Dr. Albert Schneider, yield from 50 to 100 per cent. more alkaloid than the ordinary commercial European product, and bring a correspondingly higher price. In considering the properties of belladonna, then, we may restrict our attention to those of the alkaloid atropine.

Atropine or Atropina ($C_{17}H_{23}NO_3$).—"An alkaloid obtained from belladonna. As it occurs in commerce, it is always accompanied by a small proportion of hyoscyamine extracted along with it, from which it cannot be readily separated." (U. S. P.) It occurs in white, acicular crystals, or as a fine white powder, odorless, bitter, and acrid, becoming yellowish on exposure. It is soluble in water to the extent of nearly four grains to the ounce, and freely soluble in alcohol, as well as in fifty parts of glycerin. It readily forms salts. Chemically, it is a compound of the alkaloid tropine (which lacks the properties of atropine) and tropic acid. Hence alkalies, besides acting as precipitants, as in the case of other alkaloids, may take away the tropic acid and convert the atropine into inactive tropine. Decomposition also occurs if it be heated with water or acids.

Action.—Atropine has no action upon the unbroken skin unless absorption occur. Its tendency to absorption is very slight, but can be increased by inunction or to an uncertain extent by application in the form of a plaster, for a continuous period, under the influence of the heat and confinement and the friction resulting from natural movements. Mixing it with glycerin or with alcohol or other volatile substance also leads to its absorption. It will then act both locally and systemically, and more or less poisonous symptoms can be thus induced. Its local action, applied thus or to a denuded surface, or injected into the tissues, is that of a paralyzant of the nerve endings, especially the sensory. When pain is present, this sensory depression is increased by the lessened irritation due to slightly decreased muscular movement. The systemic effects will be considered later. The local effects upon mucous membranes are also slightly benumbing, due to sensory paralysis, and inhibitory of the secretions, through paralysis of the nerve endings which excite them. The local effect in the eye is to paralyze the endings of the third nerve, thus allowing the iris to relax, producing wide dilatation of the pupil, and also to destroy the power of accommodation.

The direct systemic effects are entirely upon the nerve tissues, more upon the periphery than upon the centers. The central effects are, moreover, for the most part, rendered inoperative in the net practical results observed, because the peripheral actions are antagonistic to, and more than sufficient to overcome

them. Of the centers, the highest are affected most and the lower successively less. The primary effects upon the centers are stimulant, the secondary depressant. The most prominent, therefore, is cerebral stimulation, excitement or delirium. Even in the mildest case, the stimulation can be seen to be of an intoxicant or uncontrolled character. The cardiac centers, both vagus and accelerator, are stimulated. The first result, through the vagus, is a slowing of the heart, which almost at once yields to a quickening, at first probably through the accelerator stimulation, afterward by the secondary depression of the vagus, and lastly, as a result of depressant action on the vagal endings. The vasomotor centers are stimulated, with a brief rise of blood pressure; this is quickly overcome, chiefly by the peripheral effects, but partly by the secondary depression of the centers. Some claim also that the secondary dilatation of the vessels is due to direct stimulation of the dilator centers, but this action would probably be very brief. The respiratory centers are stimulated, with quicker and deeper breathing at first, followed by reverse conditions. The heat centers are stimulated, and there is a rise of temperature. As heat loss by evaporation of perspiration is wanting, this central action is not fully counteracted at the periphery, even though the superficial vessels are dilated; thus the rise of temperature is maintained.

The peripheral effects of atropine, for the most part, counteract and overcome the central. They are of a paralyzing nature, and relate both to movement and secretion. In regard to movement, inhibitory endings may be paralyzed so as to allow a result which is but apparent stimulation, as in the secondary quickening of the heart due to paralysis of the vagal ends, and the permission of an increase in persitalsis, due to paralysis of the splanchnic terminations. The latter action results in a laxative effect upon the bowels.

The same effect is produced upon the eye as results locally, as above described. All the buccal secretions are checked, and the mouth and throat are made dry. The pancreas secretion is similarly checked. The effect upon the production of respiratory mucus is the same as that upon the buccal, and the air passages become comparatively dry. Thus it may be sedative to respiratory irritation; but the effect is apt to be very transient. The same drying effect is produced upon the skin. The skin is red, however, from vascular dilatation, resulting from paralysis of the motor nerve endings in the arterial muscular fibers. This reddening is sufficient to produce a scarlatina-like flushing which has led to errors of diagnosis. Atropine has a strong tendency to dry up the milk.

Most of the therapeutic actions of belladonna are explained by the above pharmacodynamic deductions. Some, however, are still puzzling.

The local uses of belladonna are of almost as great importance as the internal. Prominent among them are the uses of atropine in the local treatment of the eye. The dilatation of the pupil by it permits of intraocular examination, checks iritic adhesions or breaks them down if formed, and checks ocular hernia. These results are accompanied by a lessening of pain and even a reduction of inflammation.

Many forms of superficial and some deeply seated pains, as rheumatism and neuralgia, are sometimes relieved by the belladonna plaster, or by the liniment well rubbed in, or by a solution in chloroform or camphor. Cardiac and respiratory pains are often relieved similarly. Toothache may be relieved by direct application of atropine to the nerve. Many forms of itching are promptly relieved and local inflammations scattered. Pain from hemorrhoids is partly relieved. The checking of the milk secretion can sometimes be produced by local application of the plaster. Application of a solution of atropine will often check local perspiration, though it is quite uncertain. In the nature of local applications may be regarded the intramuscular or deep injection of atropine, often combined with morphine, to relieve pain or spasms which cannot be modified by its superficial application. Inhalation of a spray containing atropine, for the relief of asthma, may also be regarded in the same light.

Internally, belladonna is probably more often used, in large doses, to check incontinence of urine, and as an adjunct of cathartics or laxatives, than for anything else. While it alone may act as a laxative, it is very uncertain. Continually used, especially together with nux vomica, it may overcome chronic constipation. Next in importance is its use in respiratory diseases, where it has a wide field of usefulness. In asthma, it often gives relief when nothing else will, and by varying its use with that of its related alkaloids permanent benefit may be secured. A similar benefit may result from its use in whooping-cough.

It checks excessive secretion, especially from the nose. With this result, irritable cough (of suitable causation) is greatly relieved. It is an excellent remedy for relieving the sweats of phthisis. Sore throat, unless of the excessively dry variety, is very favorably influenced. Cardiac inflammation or pain is benefited by its internal administration, as well as by local application. Belladonna is a useful antidote to poisoning by morphine.

The official preparations of belladonna leaves are the extract, of which the dose is 0.008 to 0.03 grams (gr. $\frac{1}{8}$ to $\frac{1}{2}$), and the fifteen per cent. tincture, dose 0.3 to 2.0 c.c. (ɱv. to xxx.). Of the extract, there is a ten-per-cent. plaster and a twenty-per-cent. ointment. Of the root there is a fluid extract, dose 0.06 to 0.2 c.c. (ɱi. to ij.), and of this we have a liniment, ninety-five parts with five parts of camphor. Children bear larger doses of atropine or belladonna, proportionally to their age, than adults.

Commercial belladonna plasters are usually made either from belladonna root, to overcome the disagreeable stain and odor of the leaf extract, or from the rhizome of scopola. Probably the very great bulk of them is made from the latter. H. H. Rusby.

Bellini, Lorenzo.—Born in Florence, Italy, Sept. 3, 1643. He began the study of medicine in Pisa at an unusually early age. Before he reached his twentieth year he had already published (Florence, 1662) an account of his very interesting researches relating to the structural anatomy of the kidneys. A short time afterward he was chosen Professor of Anatomy at the University of Pisa, and he filled that position with distinction during a period of thirty years. His death occurred in Florence on January 8, 1704.

Bellini occupies a distinguished rank in the history of medicine, not merely as an anatomist, but also as a practitioner of the art. He was the chief physician of the Grand Duke, Como III., and, at the suggestion of Lancisi, physician-in-ordinary of Pope Clement XI., he was made chief consultant of his Holiness. His principal writings have been published in two volumes, under the title of "Bellini Opera Omnia," Venice, 1708. A. H. B.

Bellocq, Jean-Jacques.—Born in Saint-Maurin, France, in 1732. In 1751 he visited Paris and devoted himself for three years chiefly to the study of surgery and midwifery. In 1774 he was given the position of lieutenant to the Surgeon-in-Chief of the king. He died on December 28, 1809.

Bellocq is known to modern surgeons through the fact that he invented a hollow sound or cannula which still bears his name. A. H. B.

Bends.—A relatively mild form of compressed-air illness occurring in caisson workers. The term is also

employed as a synonym of caisson disease as a whole. It is believed by some that "bends" in the restricted sense of the term is not a mild degree of the severe and fatal forms of caisson disease but a condition *sui generis*. The symptoms, while showing considerable variation, may be briefly described as severe muscular and articular pains in the extremities, attended by more or less muscular weakness. The descriptive term "bends" implies that the limbs are commonly flexed as a result of the attack, but this flexion does not necessarily take place. The date and place of the introduction of the word are not accurately known, but the condition is said to have existed among the caisson workers who were active in the construction of the East River or Brooklyn Bridge and the Mississippi bridge at St. Louis and who may have coined the name. The first mention of the term by a medical man seems to have been in 1882 by Broughton, who states that it was at that time of common occurrence in the newspapers. (See *Caisson Disease.*) E. P.

Benedict's Syndrome.—This is one of the characteristic syndromes of disease of the midbrain. The peculiar symptomatology may follow a variety of destructive lesions of certain areas in these parts. It may follow an infectious thrombus, an endarteritis syphilitica or sclerotica, a tumor, tuberculosis, etc. Four characteristic syndromes are described for lesions of the midbrain—they are simply the more pronounced of a list of slightly varying syndromes.

The Weber syndrome is the basis of the Benedict syndrome. The former consists of a hemiplegia of one side with an oculomotor palsy of the other. It is usually due to a disorder within the cerebral peduncles, usually at the lower end about the level of the red nucleus. In Benedict's syndrome there is added to the Weber syndrome a tremor on the paralyzed side. This tremor is usually a cross between a paralysis agitans and a multiple sclerosis, in that it is persistent, and it also has a slight intention quality to it. Benedict described his first case under the caption Paralysis Agitans.

The lesion occupies a site partly coinciding with that of the Weber syndrome, but also probably involves the red nucleus as well. (See *Brain: Midbrain Diseases.*) Smith Ely Jelliffe.

Benné Oil.—Oleum Sesami; *Teel Oil.* A fixed oil expressed from the seeds of *Sesamum indicum* L. (fam. *Pedalineæ*).

The benné plant is an erect, hairy annual, two to four feet high, supposed to have originated in Africa, but so long and so widely cultivated that knowledge of its nativity has been lost. It has been grown for its edible seeds, and for their oil, of which the yield is sixty or seventy per cent., and which is used as food and for many other purposes. The plant is grown to some extent in our Southern States. The oil is yellow or yellowish, inodorous, and of a pleasant, nut-like flavor. Its specific gravity is 0.919 to 0.923 at 15° C. At – 3° C. (26.6° F.) it becomes thick, and at – 5° C. (23° F.) it congeals. Concentrated sulphuric acid converts it to a brownish-red jelly. Its properties are purely nutritive and demulcent.

H. H. Rusby.

Fig. 637.—Level of Midbrain involved in Benedict's Syndrome.

Bennet, James Henry.—Born in 1816 in Manchester, England. He received his medical education in Paris (M. D. in 1843) and afterward began to practice his profession in London. During the early part of his career he continued to reside in that city, devoting himself largely to obstetrics and gynecology; but after 1869 he spent his winters regularly in Mentone, in the southeastern part of France. His death occurred in August, 1891.

Bennet is known to the medical profession on this side of the Atlantic almost exclusively as a charming writer on climatology and climatotherapeutics. His

principal publications on these topics are the following: "Winter and Spring on the Shores of the Mediterranean; or the rivieras of Italy, Spain, Sardinia, Malta, Corfu, Corsica, Sicily, Algiers, and Tunis as winter climates," 5th edition, 1875; "Researches regarding the Treatment of Pulmonary Phthisis," 3rd edition, 1878; "La Corse et la Sardaigne," Paris, 1876. A. H. B.

Bentley Springs.—Baltimore County, Maryland.

POST-OFFICE.—Bentley Springs.

These springs are situated on the line of the Northern Central Railroad, a division of the Pennsylvania Railroad, about thirty miles from Baltimore and seventy miles from Washington. The elevation above tide water is about six hundred feet. In addition to the two principal springs there are perhaps as many as one hundred others, some of which have important chalybeate properties. The surroundings of the springs are very interesting and attractive. The following analyses of two of the chief springs are by Professor Aiken, formerly of the University of Maryland:

THE "NUCTA" OR "STATION" SPRING.
ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Calcium carbonate	0.34
Sodium carbonate	.37
Magnesium carbonate	.27
Calcium sulphate	.30
Sodium chloride	.19
Silicic acid	.33
Iron (a trace) | Alumina and loss	.02
Total mineral contents	1.82
Organic matter	.36
Total solid contents	2.18

THE LOWER SPRING.

Solids.	Grains.
Calcium carbonate	0.64
Magnesium carbonate	.68
Sodium carbonate	.46
Iron carbonate	.89
Sodium chloride	.27
Calcium sulphate	.35
Silicic acid	.43
Alumina and loss	.03
Inorganic contents	3.75
Organic matter	0.91
Total contents	4.66

The water is a mild example of the alkaline-saline-calcic class. It has been used for upward of thirty years, in kidney, liver, and stomach disorders, and in chronic bowel affections. It is used commercially.
EMMA E. WALKER.

Benzacetine.—Acetamido-ethyl-salicylic acid, $C_6H_3NHCH_3CO.OC_2H_5.COOH$. This occurs in colorless crystals which are almost insoluble in water and have a melting point of 205° C. (401° F.). Frank introduced it as a sedative and antineuralgic said to be of special value in cases of migraine. The dose is gr. viij. to xv. (0.5–1.0), which may be repeated in one hour if necessary. W. A. BASTEDO.

Benzanilide.—Phenylbenzamide, benzoylanilide, $C_6H_5.NHCO.C_6H_5$, obtained by the action of benzoic anhydride on aniline. It occurs in small, white, shining scales, tasteless, odorless, insoluble in water, soluble in alcohol, 1 in 60. It is chemically and therapeutically allied to acetanilide. The advantages claimed for it are that it possesses less toxic properties and after its use the rise of temperature is more slow; but it has failed to become a popular remedy. It does not cause any disturbance of respiration or of digestion. The circulation is slowed, the vascular tension being reduced. In poisonous amounts it produces collapse, resembling in this respect acetanilide. In some cases large doses have altered the color of the urine, rendering it of a greenish tinge, which is increased after exposure to light. It has been recommended especially for use with children. The adult dose is gr. x. (0.6). T. L. S.

Benzene.—See *Benzol*.

Benzin.—Under the title of *Benzinum*, the United States Pharmacopœia makes official the substance commonly known as *petroleum benzin* or *petroleum ether*. It is thus defined and described: "A distillate from American petroleum, consisting of hydrocarbons, chiefly of the marsh-gas series [C_5H_{12},C_6H_{14}, and homologous compounds]. Benzin should be carefully kept in well-stoppered bottles or tin cans, in a cool place, remote from lights or fire. A transparent, colorless, diffusive liquid, of a strong characteristic odor, slightly resembling that of petroleum, but much less disagreeable, and having a neutral reaction. Specific gravity: 0.638 to 0.660 at 25° C. (77° F.). Boiling point, 45° to 60° C. (113° to 140° F.). Insoluble in water; soluble in about six parts of alcohol, and readily soluble in ether, chloroform, benzol, volatile oils, and fixed oils with the exception of castor oil. Benzin is highly inflammable, and its vapor, when mixed with air and ignited, explodes violently." (U. S. P.)

Much confusion arises from the similarity in name and general appearance between this substance—a mixture of hydrocarbons of the marsh-gas series—and the chemical body *benzene* or *benzol* (C_6H_6), a single hydrocarbon of the aromatic series (see *Benzol*). The two articles must carefully be distinguished.

Benzin is not used in medicine, but is useful to the pharmacist for its solvent powers over fats, resins, volatile oils, and other bodies.

Benzinum Purificatum.—Purified Petroleum Benzin was introduced into the eighth revision of the U. S. P. so as to provide a solvent which would not communicate a disagreeable odor to preparations such as is the case when ordinary benzin is used. It is also officially used in the preparation of deodorized opium, tincture of deodorized opium, and tincture of lactucarium.
EDWARD CURTIS.
R. J. E. SCOTT.

Benzoic Acid and Benzoates.—*Benzoic Acid*, $C_6H_5.COOH$, once known as *flowers of benzoin*, is a monatomic acid of the aromatic series, existing ready formed in a number of balsams and gum resins, notably in benzoin, and also easily obtainable, artificially, by decomposition of hippuric acid or of derivatives of toluene or of naphthalin. The benzoic acids of commerce are derived from all these sources. Benzoic acid from benzoin is characterized by a special degree of lightness and puffiness, and by a distinct benzoin odor. The acid derived from hippuric acid is manufactured out of the urine of cows and horses, and formerly was distinguishable by a urinous odor, but as at present made is quite pure and entirely free from such smell. The acid from this source is commonly known, commercially, as *German benzoic acid*.

Benzoic acid is official in the United States Pharmacopœia under the title *Acidum Benzoicum*, Benzoic Acid. The source of the article is not prescribed, but the acid is said to be "obtained from benzoin by sublimation, or prepared artificially." Although no men-

tion is made of the German acid manufactured out of horse urine, yet it is proper to say that the article so derived, if free from smell, is perfectly pure and decent for medical use. A benzoic acid made from toluene, and having an odor like that of bitter almonds, is probably not pure, and such a sample should be rejected. Benzoic acid is described officially as follows: "White or yellowish-white, lustrous scales or friable needles, odorless, or having a slight, characteristic odor resembling that of benzoin, and an acid pungent taste, somewhat volatile at a moderately warm temperature, and acquiring a yellow color on exposure to light. Soluble in 281 parts of water, and in 1.8 parts of alcohol at 25° C. (77° F.); in 15 parts of boiling water, and in 1 part of boiling alcohol. Also soluble in 3 parts of ether, 7 parts of chloroform, and readily soluble in carbon disulphide, benzene, fixed and volatile oils, but sparingly soluble in benzin. Benzoic acid volatilizes freely with the vapor of water. On heating it to 100° C. (212° F.), it begins to sublime. At 121.4° C. (250.5° F.) it melts, and at a higher temperature it is consumed without leaving a residue. The acid sublimed from benzoin has a lower melting-point and a greater solubility in water, than that prepared artificially." (U. S. P.)

Benzoic acid "should be kept in dark amber-colored, well-stoppered bottles, in a cool place." As to effects upon the animal system, benzoic acid is locally irritant to sensitive surfaces, its concentrated vapor, if inhaled, causing violent sneezing and coughing, and even bronchial inflammation. Yet, when swallowed, benzoic acid is singularly innocent. Even gram doses cause but a feeling of abdominal warmth and increase of bronchial mucus, and serious derangement is scarcely possible by any likely dosage, intentional or accidental. The action of benzoic acid, of interest in medicine, is upon the urine. Under the influence of the drug, given by the mouth, an acid urine tends to be of increased acidity, an alkaline to become acid, and a urine prone to decompose before voidance to lose such tendency. The increased acidity of urine determined by benzoic acid is mainly accounted for by the presence in the secretion of hippuric acid, undoubtedly derived, by chemical change, from the benzoic acid itself. This conversion of benzoic into hippuric acid is probably wrought in the kidneys (Meissner and Shepard). Arrest of putrefaction in urines by benzoic acid is probably simply an example of the general antiseptic action of the drug. Opposite statements have been made by investigators concerning the influence of benzoic acid, taken medicinally, upon urinary excretion of urea and uric acid, some finding the proportion of one or other of these excreta to be lessened, and others observing the same to be unaffected.

Besides the action upon the urine, benzoic acid is important for its antiseptic power, in which it probably stands on a par with salicylic acid.

The therapeutic applications of benzoic acid are principally the internal giving of the acid under its own form for the acidifying of the urine in cases in which that secretion tends to be alkaline and unduly phosphatic, or for the prevention of decomposition of the urine in the bladder in cases of vesical catarrh. The acid may also be used as an antiseptic. In saline combination, principally as sodium benzoate, benzoic acid has also been employed in acute rheumatism, as an innocent but therapeutically effective substitute for salicylic acid or the salts thereof (Senator), and in pulmonary consumption, diphtheria, scarlet fever, and other diseases of that category. In these applications, however, the reputation of the medicine is, at the present writing, decidedly on the wane.

For its legitimate use in urinary disorders, benzoic acid may be given several times daily in doses of from 0.65 to 2.00 grams (gr. x. to xxx.), administered in pill form, with soap as the excipient, or given in mixture. The Pharmacopœia gives the average dose as 0.500 grams or seven and one-half grains. Free solution of benzoic acid in water can be determined by the addition of four parts of sodium phosphate or one and a half parts of borax. Solutions for antiseptic purposes should range from two-per-cent. strength upward, solution in water being effected by the additions just cited.

Benzoates.—Such of the benzoates as are used in medicine are employed for the sake of the benzoic acid of their composition. Their discussion, therefore, belongs to this place. The benzoates official in the United States Pharmacopœia are the *sodium*, *lithium*, and *ammonium* salts.

Sodium Benzoate, $C_6H_5.COO.Na$.—This salt is official as *Sodii Benzoas*, Sodium Benzoate, and is described as "a white, amorphous granular or crystalline powder, odorless, and having a sweetish astringent taste. Permanent in the air. Soluble, at 25° C. (77° F.), in 1.6 parts of water and in 43 parts of alcohol; in 1.3 parts of boiling water, and in 12 parts of boiling alcohol. When heated, the salt melts, emits vapors having the odor of benzoic acid, then chars, and finally leaves a residue of sodium carbonate and carbon. To a non-luminous flame it imparts an intense yellow color. Its aqueous solution is neutral or slightly alkaline to litmus paper." (U. S. P.) The salt should be kept in well-stoppered bottles. Sodium benzoate is made by treating a sodium carbonate, in hot saturated aqueous solution, with benzoic acid, and the quality of the salt will be determined by the quality of the benzoic acid used in its manufacture. The article described by the Pharmacopœia is intended to be made from benzoin-benzoic acid. Specimens made from hippuric-benzoic acid and from toluene-benzoic acid have been found to be less freely soluble in water than the above, and to yield pale yellow and turbid solutions of an acrid, bitter taste, and of an odor of horse sweat or of bitter almonds, according to the source of the benzoic acid.

Physiologically, sodium benzoate is about as harmless as a salt can be, but has been found to produce fully the curative action of benzoic acid itself in acute rheumatism, and has been loudly vaunted as of wonderful avail in pulmonary consumption, diphtheria, etc. It has been given internally in doses amounting to from five to twenty grams (gr. lxxv. to ʒv.) a day, without serious derangement, and for pronounced effect in acute rheumatism the fullest limit of such dosage may be necessary. The Pharmacopœia gives the average dose as one gram or fifteen grains. In diphtheria, inhalations of atomized spray and insufflations of the powdered salt upon the diphtheritic patch have also been practised.

Lithium Benzoate, $C_6H_5.COO.Li$.—The salt is official as *Lithii Benzoas*, Lithium Benzoate. It is thus described: "A light, white powder, or small, shining crystalline scales; odorless, or of faint benzoin-like odor, and of a cooling, sweetish taste; permanent in the air. Soluble at 25° C. (77° F.), in 3 parts of water, and in 13 parts of alcohol; in 2.5 parts of boiling water, and in 10 parts of boiling alcohol." (U. S. P.) The presence of sodium benzoate increases the solubility in water and lessens that in alcohol.

Lithium benzoate is made by direct decomposition of lithium carbonate by benzoic acid; and, as in the case of the making of sodium benzoate, benzoin-benzoic acid should be used for the manufacture.

Lithium benzoate is an innocent salt, seemingly yielding to a certain degree similar results to benzoic acid itself in urinary affections (see under Benzoic Acid, *ante*). It has been used in such conditions in the place of the uncombined acid, in doses of from one to two grams (gr. xv. to xxx.) several times daily. The Pharmacopœia gives the average dose as one gram or fifteen grains.

Ammonium Benzoate, $C_6H_5COONH_4$.—The salt is official as *Ammonii Benzoas*. Ammonium Benzoate. It is thus described: "Thin, white laminar crystals, or a crystalline powder; odorless, or having a slight odor of benzoic acid, a saline, bitter, afterward slightly acrid taste, and gradually losing ammonia on exposure to the air. Soluble at 25° C. (77° F.), in 10.5 parts of water and in 25 parts of alcohol; in 1.2 parts of boiling water and 7.6 parts of boiling alcohol." (U. S. P.) The salt is made by adding benzoic acid to water of ammonia, and, as in the case of the other benzoates, benzoin-benzoic acid should be used in the making. The benzoate should be kept in well-stoppered bottles.

Ammonium benzoate is an innocent salt, and affects the urine after the manner of benzoic acid itself. It is used in place of the acid in urinary disorders (see Benzoic Acid, above), in doses of from one to two grams (gr. xv. to xxx.) several times daily. The Pharmacopœia gives the average dose as one gram or fifteen grains. It amounts, medicinally, to a soluble form of benzoic acid, and can readily be made extemporaneously in solution by saturating benzoic acid with water of ammonia. Let the amount of benzoic acid to be prescribed be mixed with a little water, then neutralized with water of ammonia, and the whole brought to a desired volume of solution by further addition of water (Squibb).

EDWARD CURTIS.
R. J. E. SCOTT.

Benzoin.—BENZOINUM, *"Gum Benjamin."* "A balsamic resin obtained from *Styrax benzoin* Dryander and another unidentified species of *Styrax* (fam. *Styraceæ*)." (U. S. P.) The tree here named is known to be the source of the *Sumatra* variety of benzoin, but is probably not that of the *Siam* variety. It is a good-sized tree, rather widely distributed through the East India Islands, and to a considerable extent cultivated in Sumatra. At the age of about six years, when the tree is six to eight inches in diameter, collections begin. They are continued for from fifteen to twenty years, the product becoming darker and more inferior with each succeeding year. The sap exudes from incisions made for the purpose, as a milky juice which is collected in tears, at first whitish, then becoming yellow, or rusty brown, but still milky white when fractured. If this concrete product of the young trees is packed separately, it results in a more or less loosely constructed cake, of excellent quality. Ordinarily, however, there is a considerable quantity, often very large, of a darker substance which, run, or perhaps kneaded, into the interstices, and then hardening, converts the contents of the boxes in which it comes packed into a solid mass of a pinkish or reddish gray, or of a gray or sometimes gray-brown color, in which the white or yellowish tears are firmly embedded. It is believed that this interstitial substance consists of the soft product from old trees, or even of a very inferior substance obtained by barking and scraping the trunks. Even this inferior variety may be regarded as good in comparison with the very large quantity of adulterated benzoin which reaches us. Adulteration was formerly practised by embedding large stones in the center or ends of the mass, but the inspection of the blocks by splitting them diagonally in various directions checked this, and recourse is now had to fine gravel, sand, or other earthy matter, for the purpose. Benzoin thus adulterated is called "drossy." Large amounts of bark, wood and other vegetable tissue are often present. Benzoin, when cold, breaks with a sharp, brittle fracture, and a shining or sparkling surface, but becomes more or less plastic or adhesive in a warm atmosphere. It has a very pleasant balsamic odor and a rather mildly aromatic, somewhat acrid and unpleasant taste. Benzoic acid sublimes from it. Five parts of warm alcohol should dissolve nearly all of it, if pure.

Siam benzoin is packed in similar boxes, but consists of a porous mass of tears only, loosely cohering or separate. These tears are known in trade as "marbles" or "almonds" and the respective grades are known as "large" or "small marbled." The outer surface of these tears becomes of a darker yellow or brown than the Sumatra, but they also are white internally. They are much more fragrant, reminding one somewhat of vanilla. This variety is much more expensive than the Sumatra, and is little subject to adulteration.

The principal constituent of benzoin, as to percentage, constituting almost the whole of it, is resin, but its active constituent is benzoic acid, which see. There is a little volatile oil, and usually a trace of cinnamic acid. Both varieties contain vanillin, the Sumatra usually considerably less than one per cent., the Siam often one and a half per cent. or more. Styracin is usually present in the extent of two or three per cent. and these are various cinnamic and benzoic compounds.

Action and Uses.—So far as the medicinal action and use of benzoin is concerned, it is identical with benzoic acid, in proportion to its percentage. Otherwise it is used in pharmacy for perfuming medicinal substances or for rendering them antiseptic, and very largely in the manufacture of perfumery. The official preparations are the *Adeps Benzoinatus*, or *benzoinated lard*, which contains two per cent. of it; the tincture, of twenty-per-cent. strength, which is the distinctly medicinal preparation, the dose 2 to 4 c.c. (fl. ʒss. to i.); and the compound tincture or "Friar's Balsam," containing twelve per cent. of benzoin, eight per cent. of storax, four per cent. of balsam tolu, and two per cent. of purified aloes, the dose being the same as of the last. HENRY H. RUSBY.

Benzol.—This substance, formerly called *benzene*, is the simplest hydrocarbon of the aromatic series, having the formula C_6H_6. It is thus a definite chemical compound, and must carefully be distinguished from *benzin* (*q.v.*), a composite substance obtained as a distillate from coal oil. Benzol or benzene is a thin, colorless fluid, very volatile and very inflammable, and, when pure, of a not disagreeable aromatic odor. It is practically insoluble in water, but dissolves in four parts of alcohol. It may be obtained by distilling a mixture of benzoic acid and lime, or by fractional distillation of the material known as *coal naphtha*, a derivative of coal tar.

Benzol is of more value in pharmacy than in medicine. For pharmaceutical purposes it is notable for its extensive solvent power, dissolving readily such comparatively insoluble substances as india rubber, guttapercha, sulphur, phosphorus, and iodine; many resins and alkaloids also dissolve readily in it. Physiologically, benzene has little local effect, but taken internally determines intoxication, coma, and anesthesia. It has been given internally in doses of a few drops in dyspepsia associated with fermentation of the ingesta, and also in trichinosis, but is rarely employed and is not official in the United States Pharmacopœia. EDWARD CURTIS.
R. J. E. SCOTT.

Benzonaphthol.—See *Betanaphthol Benzoate.*

Benzo-phenoneid.— Tetra-methyl-diapsido-benzophenoid. A non-irritating though powerful germicide, obtained by the decomposition of an aniline dye. It is similar to pyoktanin, is soluble in 100 parts of water, and is not caustic. Like yellow

pyoktanin it has been used in corneal ulcers, pustular keratitis, and various ulcerative lesions of the skin and mucous membranes.

W. A. Bastedo.

Benzosulphinidum.—The official (U. S. P.) name of the product commonly known as saccharin; the official name in the British Pharmacopœia is *Glusidum* or glucusimide. This is a coal-tar product, a derivative of toluene, with the formula $C_6H_4(CO)(SO_2)NH$. It occurs as a light white powder, odorless, but with an intensely sweet taste. It is very slightly soluble in cold water, more so in boiling water, alcohol, and glycerin. Its solution gives an acid reaction, and it forms with alkalies sweet salts which are freely soluble. The sodium salt is the saccharin of commerce. It may be prepared by dissolving 100 parts in water and neutralizing the solution with bicarbonate of sodium and evaporating to dryness; this forms 113 parts of soluble gluside or saccharin.

Except in its sweetening power, saccharin is not allied to sugar in any way. It does not affect polarized light, it lacks the essential character of sugar to produce alcohol by fermentation, and when administered does not increase the production of sugar in the system. It is this latter quality that renders it of value in the dietary of diabetes, where it is desired to avoid the use of sugar.

Saccharin is nearly 500 times as sweet as sugar. One-half grain being equal to an ordinary lump of white sugar. By improvements in the process of manufacture the degree of sweetness has been greatly increased. Formerly it was a mixture of para- and ortho-salts; the former a tasteless salt, is now entirely removed. Its disadvantages are the distaste that the patients are liable to have for it after continuing its use for a time, and the dry, acrid sensation which it sometimes produces in the pharynx.

In medicines it may be used to replace sugar and syrup for the purpose of rendering them palatable, one grain with a six-ounce mixture furnishing sweetness equal to one ounce of ordinary syrup. To facilitate dispensing, the following solutions are prepared:

Liquor Saccharini (National Formulary): Benzosulphinidum, 512 grains; bicarbonate of sodium, 240 grains; alcohol, 4 fluidounces; water, sufficient to produce 16 fluidounces. Each dram represents four grains of saccharin.

Elixir Glusidi (Unofficial Formulary of the British Pharmaceutical Conference): Gluside, 480 grains; bicarbonate of sodium, 288 grains; rectified spirit 2½ fluidounces; distilled water, enough to make 20 ounces. Each dram represents three grains of gluside.

Saccharin may be given freely; in some cases reported its prolonged use has produced symptoms of gastric disturbance with indigestion, but this rarely occurs.

Saccharin possesses antiseptic properties in common with other coal-tar derivatives, and for this reason it has been suggested as a remedy in many diseases. It has been used in pulmonary phthisis, acute articular rheumatism, scarlatina, intestinal catarrh, cystitis, and a number of other disorders in which its antiseptic action might prove of service. Of these, cystitis is the only one in which any satisfactory results have been obtained. In this condition it is administered internally and renders the urine antiseptic during its excretion. When there are pus and an alkaline reaction, this is rapidly overcome, and the urine becomes clear and normal in character; the change in the urine being accompanied by a corresponding improvement in the mucous membrane of the bladder. Three grains, in divided doses, daily, is the quantity recommended, this is to be continued for a prolonged period.

Beaumont Small.

Benzoyl-eugenol. — $C_6H_3.C_3H_5.OCH_3.OCOC_6H_5$. This is a combination of benzoic acid and eugenol, combining the antiseptic properties of oil of cloves with those of benzoic acid. It occurs in large colorless prisms or in small needle-shaped crystals, is odorless and tasteless, insoluble in water, and freely soluble in alcohol, ether, chloroform, and acetone. It is an intestinal antiseptic, and being to some extent eliminated by the bronchial mucous membrane, it may act as a stimulant and antiseptic to the respiratory tract. So far its use has been confined to cases of pulmonary and intestinal tuberculosis. Dose, gr. vij. to xv. (0.5–1.0) in powder or capsule, or mixed with milk.

W. A. Bastedo.

Benzoyl-tropeine. — $C_8H_{11}C_6H_4CONO$. Tropine, the mother substance of atropine, is heated to 100° C. with benzoic and dilute hydrochloric acids. The resulting silky needles constitute benzoyl-tropeine. They are insoluble in water, have a strongly basic reaction, and with acids form soluble salts. This compound seems to stand chemically between cocaine and atropine, and it partakes of the nature of each. Thus Filehne found it to be a valuable local anesthetic when applied to the eye, it at the same time causing dilatation of the pupil. Its exact pharmacology has not been studied. The soluble salts may be used in one to four per cent. solution.

W. A. Bastedo.

Berberine.—$2(C_{20}H_{17}NO_4+9H_2O)$. An alkaloid obtained chiefly from *Berberis vulgaris* L., but very common in other plants, especially in the families *Berberidaceæ*, *Ranunculaceæ*, and *Menispermaceæ*. It occurs in yellow, needle-shaped crystals, or as a yellow crystalline powder, and is soluble in alcohol and hot water. It forms numerous yellow crystalline salts. It is not poisonous. Aside from its effects as a simple bitter, its physiological action is rather weak. It is somewhat stimulant to unstriped muscular fiber, yet it causes a fall of blood pressure and slightly lowers the temperature. Large doses are irritant and may produce purgation. It is usually given as the sulphate. The dose as a tonic is 0.03 to 0.06 gram (gr. ss. to i.). Doses of ten to fifteen times these amounts are antiperiodic.

Henry H. Rusby.

Berberis.—*Oregon Grape root, Barberry.* The rhizome and roots of *Berberis aquifolium* Pursh or of other species of *Berberis* Linne. (Fam. *Berberidaceæ*.) (U. S. P.) The genus Berberis contains more than 100 species, very widely distributed throughout the north temperate zone and extending along the mountains into and through the tropics. They are beautiful erect or prostrate, yellow-flowered shrubs or small trees, the evergreen leaves mostly pinnate and usually spinulose-toothed. All parts are permeated by the alkaloid *berberine*, the largest percentage occurring in the bark, and more particularly in that of the root. In most places where the species grow they have gained a high reputation as bitter tonics.

B. vulgaris L. is an erect species of Europe and adjacent Asia, naturalized to some extent in North America, its scarlet fruit largely used in olden times as cranberries now are. Both the root and the bark have long been used medicinally as an antiperiodic, febrifuge, and tonic. Besides the berberine, it contains the alkaloids oxyacanthine and berbamine. Oxyacanthine is at first white, but turns yellow on exposure to light. The two last-named alkaloids apparently do not exert much influence, as the action of berberis is practically that of its berberine.

B. aquifolium Pursh, Oregon grape root or mountain grape, is a low, diffuse, blue-fruited species, very

abundant in the Northwestern United States. It and similar species of the region hold a remarkable place in the esteem of the miners and mountaineers, who rely chiefly upon this and the mountain sage (*Artemisia frigida*) in the treatment of fevers. Its constituents are about the same as those of *B. vulgaris*. The root is used. Very many reports agree in attributing to this drug, in addition to the ordinary tonic properties of a vegetable bitter, a special power in stimulating nutrition. The dose of both species is 0.2 to 0.6 gram (gr. iij. to x.). Large doses are laxative. The best form of administration is the powder, fluid extract, or tincture.

In India, *B. aristata* D.C., *B. lycium* Royle, and *B. asiatica* Roxb. are similarly employed.

HENRY H. RUSBY.

Berck-sur-Mer.—A sea-coast village of France, lying upon the shore of the English Channel. It is situated on sand dunes, and has nothing particularly attractive about it; but there is situated here, however, that which makes it worthy of mention, several sanatoria for children suffering from bone, joint, and glandular tuberculosis. The largest is the sanatorium of the "Assistance Publique de Paris" which has a capacity of from 700 to 800.

Excellent results have been obtained in such seaside sanatoria in the treatment of surgical tuberculosis in children, and similar institutions exist in various other places along the Coast of France, Holland, Belgium, Denmark, Austria, Germany, Russia and England, the one at Margate having been founded in 1796. In France alone, according to Armaingand, "60,000 children suffering from tuberculosis of the bones and glands have been treated in sea-side sanatoriums since 1887, with fifty-nine per cent. of cures and twenty-five per cent. of cases decidedly improved. The percentage of cures varied from thirty-two in Pott's disease to seventy-four in glandular tuberculosis." In about three-quarters of the cases the cures have been shown to be permanent. According to D'Espine, other countries have shown equally encouraging results "whether the sanatorium was located on the Baltic, the North Sea, the Mediterannean, the Adriatic, or the Atlantic Ocean."

At the International Congress of Tuberculosis held in Paris in 1905, marine sanatoriums for tuberculous children were fully discussed, and the conclusions of the Congress were "that the sea-shore offered special advantages for the treatment of non-pulmonary tuberculosis in children."

In this country the Sea-Breeze Hospital at Coney Island has been established for several years for the treatment of children suffering from surgical tuberculosis, and the sea-air, together with the open-air life, and a nourishing and abundant diet, have produced equally favorable results. Of twenty-three cases of hip disease, all of them advanced, forty-three per cent. left the hospital absolutely cured, and nine per cent. improved. Of knee or other joint disease, although over eighty-one per cent. were in an advanced stage, there was an average of seventy-three per cent. cured and thirteen per cent. improved; and of the glandular cases, eighty-five per cent. were either cured or improved. "It has been demonstrated," says Brannan,[1] "that to obtain the best results in the treatment of bone and gland tuberculosis it is essential that the patient should spend his entire time in the open air," and "In addition it has been shown that the seashore offers especial advantages for outdoor life in this variety of tuberculosis."

The above emphasizes the great value of sea-side residence and open-air life for children suffering from non-pulmonary tuberculosis. EDWARD O. OTIS.

[1] Transactions of the Sixth International Congress on Tuberculosis, vol. ii. p. 68.

Berengario, Jacopo.—Born at Carpi, in the Duchy of Modena, Italy, toward the end of the fifteenth century. He became distinguished for his skill as a surgeon, and between the years 1502 and 1527 he was Professor of Surgery, first at Pavia and afterward at Bologna. Fallopius and Eustachius speak of him as having done more than any of his contemporaries to revive the study of anatomy. In the earlier part of his course he was obliged to use pigs as material for dissection, but at a later period he is reported to have dissected more than 100 human cadavers. As had already happened to other zealous anatomists, Berengario was accused of dissecting human beings while they were still alive; and his accusers finally succeeded in having him driven out of Bologna. The last part of this statement is denied by some authorities; his departure for Ferrara, they claim, was due to a desire on his part to escape the persecutions of the Inquisition, whose tribunal took decided exception to his opinions with regard to the organs of generation. Whatever may be the truth in regard to the cause of Berengario's leaving Bologna, it is an undisputed fact that, from 1527 to the time of his death in 1550, he resided in Ferrara where he became a close friend of the reigning duke, probably Ercole II.

Berengario is credited with being the first physician who noted the beneficial effects of mercurial frictions in venereal diseases. This mode of treatment gave him wide celebrity and brought him a large fortune.

Of his published writings the following deserve to receive special mention: "De calvariæ sive cranii fractura tractatus," Bologna, 1518 (Leyden, 1629 and 1651); "Commentaria cum amplissimis additionibus super anatomiam Mundini, una cum textu ejusdem in pristinum, et verum nitorem redacto," Bologna, 1521 (also 1552); and "Isagogae breves perlucidæ, ac uberrimæ in anatomiam humani corporis a communi medicorum academia usitatam," etc., Bologna, 1522. A. H. B.

Bergamot, Oil of.—OLEUM BERGAMOTTÆ. A volatile oil obtained by expression from the rind of the fresh fruit of *Citrus bergamia* Risso et Poiteau (fam. *Rutaceæ*). The bergamot tree is a small evergreen, very much like the bitter orange in almost all respects, but the leaves are obovate, with narrowly winged petioles, and the flowers are smaller and fewer. It is not known in a wild state—indeed, it was not known at all until about 200 years ago, when it appeared in the south of Europe. There is no doubt it is a hybrid or cross of some kind, probably between the bitter orange and the lemon or citron. The fruit is about as large as a small orange, and has the same general structure. It is rounded pear-shaped, about as broad as long, with a broad, flat, or even depressed summit; the skin is soft, smooth, yellow, and very fragrant. The pulp is sour and bitter.

Bergamots are raised in the vicinity of Reggio, in the south of Italy, and in Sicily, and the oil is exported from Messina and Palermo. This is collected mechanically by rupturing the vesicles, sometimes by the old sponge process used with oranges and lemons in obtaining their oils, but more generally now by a sort of hand-mill, into which the fruits are put whole, and rolled and rubbed against a series of knives, which cut or scrape the surface and so liberate the oil. It flows to the bottom of the mill, and out through suitable apertures. One hundred fruits yield two and a half or three ounces of the oil (Flückiger).

It is a thin, mobile, pale-green, or greenish liquid, with a very fragrant, pleasant odor, and a bitter, aromatic taste. Its specific gravity is 0.883 to 0.886, its reaction slightly acid. Its active portion is linaloyl acetate. Like the essential oils in general, it

dissolves readily in alcohol, chloroform, ether, and fats, and only very sparingly in water. The green color is due to chlorophyll.

The medical properties of oil of bergamot are those of essential oils in general, but it is never used internally. On the other hand, its delicious odor has made it a universal favorite in perfumes and toilet preparations. The world-renowned Cologne water has it as its principal ingredient, modified by other aurantiaceous oils. There are numerous formulæ for making it; one, formerly official as *Spiritus Odoratus*, is as follows:

Oil of Bergamot	16 parts.
Oil of Lemon	8 parts.
Oil of Rosemary	8 parts.
Oil of Lavender Flowers	4 parts.
Oil of Orange Flowers	4 parts.
Acetic Ether	2 parts.
Water	158 parts.
Alcohol	800 parts.
	1,000 parts.

H. H. Rusby.

von Bergmann, Ernst.—Born in Riga, a seaport of Russia, on December 16, 1836. He received the degree of Doctor of Medicine from the University of Dorpat, in 1860. He rendered valuable professional services to the German Army during the Franco-Prussian War (1870–1871). From 1871 to 1877 he occupied the regular chair of surgery in the University of

Fig. 638.—Ernst v. Bergmann.

Dorpat. During the Russo-Turkish War (1877-1878) he acted as Consulting Surgeon of the Danube wing of the Russian Army. In 1882 he was called to Berlin to occupy the Chair of Surgery recently made vacant by the death of Langenbeck, and he continued to occupy this chair up to the time of his death, on March 25, 1907.

von Bergmann's contributions to the literature of surgery are numerous and of a very varied character. To medical men on this side of the Atlantic, however, he is chiefly known through the English translation of the "Handbuch der Speziellen Chirurgie" (by von Bergmann, von Bruns and von Mikulicz-Radecki, Stuttgart, 1899), edited by the late Dr. William T. Bull of New York. In this large work von Bergmann himself wrote the chapters on wounds of the head and on diseases of the brain. A. H. B.

Beriberi.—*Synonyms:* Berbiers, Kakké (China and Japan), Hinchazon (Spanish America). Beriberi is probably a Sinhalese word. It is said that no cases arise in Ceylon, though many are brought there in ships.

Definition.—A degenerative polyneuritis resulting from defective diet. In the most serious cases the pneumogastrics and phrenics are involved. The disease is prevalent in those countries and among those races in which rice forms a preponderating factor in the diet.

History and Distribution.—As kakké, the disease is described in Chinese writings of the second, seventh, and ninth centuries. The first European physician to describe it as beriberi was Bontius in 1758, since which time it has been extensively studied by hundreds of observers within its areas of prevalence. It is commonest in China, Japan, eastern and southeastern Asia, and the adjacent islands of Malaysia. In the year 1905, in the Straits Settlements, it caused 1,888 deaths, or nearly eight per cent. of all deaths. It has been encountered in eastern and western Africa. Cases have been seen in Canada, the United States, Central America, and Brazil.

Etiology.—Beriberi is a disease of malnutrition, a consequence of a deficient diet. This conclusion has not been reached without a vast amount of speculation, investigation, and argument in support of contending theories. Any attempt to deal at length with the many rejected theories would be a waste of time and space in a work of this kind. These theories, however, have been put forward from time to time by men whose speculations are entitled to attention. The literature in which they can be found is still recent. It seems proper, therefore, merely to enumerate some of them since many of them have had eminent sponsors. Briefly, then, beriberi has been attributed to poisoning by arsenic, by oxalates, by carbon dioxide, by fish, by rice; to antointoxication; to a bacterial infection in the body; to a bacterial toxin derived from an extracorporeal place infection (Manson); to fungi; to some protozoan infection with a possible insect-carrier; to a helminth infection.

The fact that outbreaks of beriberi occur so often in jails, asylums, and the forecastles of ships has led many observers to attach a very special importance to overcrowding, insufficient ventilation, and insanitary conditions generally, as predisposing causes.

It will be apparent that theories as to the etiology of beriberi have closely paralleled theories similarly put forward as to the etiology of scurvy. And there is a similar parallelism in the only acceptable conclusion. It is not salted, smoked, dried, tinned, or otherwise preserved food, nor any one or many kinds of food the eating of which produces scurvy. It is because the diet, whatever it may be, *lacks* some substances necessary to the maintenance of health that scurvy develops. Nothing that a man can eat will give him scurvy. And nothing that a man eats will give him beriberi. In each case it is a *deprivation*, a *lack* of substances required to make up an adequate diet for the support of health, that gives rise to disease. Upon substituting a liberal and properly varied diet for the deficient one, recovery ensues. Monteith[1] has reported an Australian epidemic of beriberi with scorbutic symptoms, and Balfour[2] has seen just the reverse in the Sudan. Bremand and Laurent, in Siam, thought that the disease is due to too little fat in the food, and believed that an epidemic was stopped by causing the healthy to eat more fat.

An analysis of the experience of the Japanese Army which had during eighteen months of 1904–05, 97,572 cases, with 3,956 deaths, showed that beriberi was almost sure to develop "when the soldier ate as much as twenty-six ounces of rice daily *and little else.*"

Prior to 1884 about thirty-three per cent. of the men in the Japanese Navy were continuously disabled by beriberi. Surgeon General Takagi reformed the ration, substituting, for ten parts of rice, seven parts of barley and three parts of rice, and adding some meat to the ration. Beriberi was completely wiped

out of the service. He concluded that the disease was caused by a deficiency of proteins in the diet. Similarly beriberi has recently almost entirely disappeared among the Philippine Scouts since legumes have been substituted for a part of the rice in their ration.

Outbreaks of degenerative polyneuritis similar to beriberi if not identical with it have been seen (1) in Brazil in a population using not rice but sago as a predominating diet factor; (2) in asylums for the insane at Dublin, Ireland, Tuscaloosa, Alabama, and Little Rock, Arkansas; (3) aboard Norwegian and other merchant vessels, and in numerous other circumstances where rice-eating was not a factor. But the striking prevalence of that peculiar polyneuritis called beriberi in countries and populations in which rice is not only a staple but forms a preponderating factor in the diet, has concentrated the attention of investigators upon rice and the various forms in which rice is marketed and eaten. The work of Fraser and Stanton in the Malay Peninsula, of Chamberlain and the Army Board in the Philippines, and of numerous investigators elsewhere, has shown that while a diet consisting largely of unmilled rice will usually sustain health in those accustomed to it, polyneuritis frequently, almost invariably, develops if milled or polished rice be substituted for the unmilled whole grain. This occurs in man, in the nursing infants of mothers so fed, and in experimental fowls. The pericarp removed by milling contains phosphates and vegetable fat in considerable amounts, and other undifferentiated organic substances. The polyneuritis does not develop, or is cured if it has developed, if the patient or fowl be fed on polished rice and receive in addition the polishings or certain fluid extracts thereof. The Dutch physicians in Java report that the proportion of cases in the prisons is one in thirty-nine when milled rice is eaten, and one in ten thousand when rice is eaten with the pericarp. But with the use of milled rice, an experimental substitution of phosphates for the polishings or their fluid extract has not availed to prevent the disease. All experiments have failed to demonstrate that the absence from the diet of phosphorus, or fat, or nitrogen, or any other definitely known substance or class of substances is the ultimate or exact cause of beriberi.

The only conclusions as to the causation of beriberi which are warranted by our present knowledge are these:

For the maintenance of health and the nourishment of all the tissues a well-balanced diet is required. Though the diet be varied and even rich, if *fresh organic matter either animal or vegetable* be entirely excluded from it, that *general dyscrasia* known as *scurvy* will ensue. Meat and other animal foods can be excluded from the diet, but if it consists of a good variety of vegetables including the legumes health will be maintained. If the preponderating factor in a diet be a breadstuff made from one of the valuable grains rich in gluten, such as wheat, rye, maize, oats, or barley, health can be maintained even though little be eaten beyond this staple. But if for one of these valuable grains there be substituted as the staff of life for any people rice, the poorest of all the cereals in protein content, we approach the danger of that *nerve-dyscrasia* known as *beriberi*. If rice, though the main, be not the only breadstuff, if some barley or others of the more valuable grains be used also, or if with rice as the only cereal, beans, or fish, or meat, or milk be added, and thus proteins, phosphates, fats, and various undetermined substances necessary to health be supplied in larger proportion than they are contained in rice, health will be maintained. Many natives of a rice-eating country will maintain health on a nearly exclusive rice diet, provided the rice be of good quality and be eaten unmilled or undermilled, that is, with its pericarp. But beriberi will develop in an enormous proportion of individuals in any rice-eating population under either one of two sets of conditions, namely: (1) if milled or polished rice is the predominating factor in the diet, or (2) if rice either milled or entire be eaten to the nearly complete exclusion of other varieties of nourishing food.

More males than females suffer from beriberi, and the majority of cases seen are in early adult life between the ages of fifteen and thirty-five.

Pathology.—Edema is probably due directly to involvement of the vasomotor nerves as well as to the pneumogastric-cardiac condition. *Post mortem* there is an early rigor mortis and usually a marked hypostasis. Examination of the nerve trunk reveals a bilateral peripheral degenerative neuritis, the extent and degree of this condition being proportioned to the duration and severity of the case. The pneumogastrics and other cranial nerves are apt to be involved. The changes in the nerves, which have been carefully studied by Scheube, Baelz, Hamilton Wright, and Dürck are summarized by Castellani and Chalmers,[3] as follows:

"The neurokeratin network becomes irregular, and its meshes wider, while its rods disappear. The medullary sheath becomes vacuolated, and its inner boundary ill-defined. In other places the neurokeratin network condenses into small rosary-like masses or larger lumps, somewhat regularly arranged. Later the medullary sheath breaks up into spherical or elongated masses separated by clear intervals. The axone undergoes first chemical changes, and then appears like a wavy cord, or as a series of comma-like segments, or twisted up into a coil. Finally both axone and medullary sheath disappear, while Schwann's sheath collapses, and so the nerve fibers become lost in the connective tissue of the endoneurium. Along with these changes there is a cellular infiltration of the perineurium, especially of the perivascular spaces, and also of the endoneurium. These cells are said to be like a similar infiltration met with in traumatic lesions of nerves, and to resemble the granule cells of the central nervous system. When fully degenerated the nerve may consist simply of connective tissue. Regeneration has not been observed, but must occur—at all events, to some extent—in cases which recover."

Changes have been described in the bulbar and ganglionic cells, but the cortical cells and the spinal cord itself are usually normal. The heart is dilated and often shows fatty degeneration, the venous system is engorged and the subcutaneous tissue edematous, and fluid is found in the serous cavities. The muscles are atrophied. In acute cases there is gastroduodenitis, sometimes with submucous hemorrhages, sometimes even with extravasation of blood into the lumen. Petechial hemorrhages may be observed elsewhere in the intestinal walls, and in the pleura and pericardium. Macroscopic hemorrhages may also be found in the liver. These hemorrhagic changes are not found in chronic cases.

The spleen and pancreas are usually normal. The liver is generally enlarged and congested. There is an interstitial hepatitis with round-celled infiltration of the connective tissue and with fatty degeneration, cloudy swelling, and necrosis of the lobular cells. Even when true hemorrhages are not present in the liver, extravascular erythrocytes are observed. This condition has been described as a "diapedesis of the red corpuscles" in the liver, and is stated to be more or less peculiar to beriberi.

There are no characteristic changes in the blood. In most of the cases there is some reduction in red cells and hemoglobin. If eosinophilia exists it is usually due to a coexistent helminth infection (hookworm, filaria, etc.).

Symptoms and Course.—A typical case of beriberi begins with malaise, anorexia, pain and tenderness in the epigastrium. Sensory changes appear early,

irregular and shifting patches of anesthesia in the extremities, pain on pressure, especially in the muscles of the calf. Motor and vasomotor changes follow, loss of power and of reflex, edema, etc. The gait is ataxic, but instead of an emphasis upon the heel in stepping there is usually foot-drop and a corresponding extensor weakness at the wrists. If the case is unrelieved muscular wasting and fat wasting ensue. If to these peripheral nerve conditions there be added as the case progresses involvement of the pneumogastrics and the phrenics, cardiac dilatation, failing circulation, dropsy, and dyspnea appear, and a large proportion of such advanced cases terminate fatally. The development of these graver symptoms may be rapid, death occurring suddenly in a case that has been regarded as mild or ordinary. The usual course is chronic, however, and terminates in recovery. In the absence of complications there is no fever. A rise of temperature is evidence of tuberculosis, malaria, dysentery, or some other complication.

The urine shows little change in mild cases. In severe cases it is at first diminished, becoming copious as the dropsy disappears.

Cases of beriberi have been divided by many writers into so-called *forms* of the disease, but the differences are those of severity and duration. Thus very mild cases with slight symptoms and rapid recovery have been called incomplete, rudimentary, ambulatory, or abortive. Those in which paralysis and wasting are marked are called dry or atrophic beriberi, and the dropsical cases are called wet or hypertrophic beriberi. And cases have been called acute, pernicious, or cardiac when the heart is involved early and death is sudden.

Diagnosis.—This is usually not difficult except to the novice in tropical medicine. I have seen a case of beriberi in a Chinaman exhibited to an American medical society as a case of "syphilis of the heart." The condition must be differentiated from organic heart disease, from alcoholic and arsenical neuritis, and from plumbism; from rheumatism with cardiac complication; from locomotor ataxia; from pellagra; from ergotism and lathyrism.

In endemic areas an early stage of the disease may be suspected from loss of appetite, tenderness over the epigastrium, and exaggerated knee-jerks. More conclusive signs as the disease advances are loss of knee-jerks, patches of anesthesia, pain on squeezing the calves, edema, heart weakness, and the absence of albuminuria and of fever.

Prognosis.—In cases of the type called pernicious, with development of grave conditions from the outset, the prognosis is always bad. Such cases are almost invariably fatal. It is unfavorable in cases with complications such as dysentery, malaria, or a serious anemia. The commonest cause of a grave anemia in these cases is a coexisting hookworm infection. Uncomplicated cases of ordinary severity usually recover, generally with an astonishing absence of the serious sequelæ which might be reasonably anticipated, such as permanent paralyses, muscular atrophy, or cardiac impairment. The mortality varies greatly; in different countries, races, and epidemics from two to seventy per cent. Favorable signs are that the heart is not much involved, and that the patient has a good flow of urine and a good appetite.

Prophylaxis.—The measures to be taken for the prevention of beriberi are sufficiently indicated by a due consideration of the causes and the nature of the disease and the circumstances under which its appearance is to be feared. Under all circumstances in which a large number of individuals, mainly dependent upon rice as a staple (or upon sago or potatoes) to the practical exclusion of any of the valuable glutenous grains, are herded together as soldiers, sailors, prisoners, or inmates of an asylum, their vitality lowered by hardship, confinement, crowding, or other insanitary conditions, and dependent upon rations issued to them by authority, care should be taken that they receive unmilled or undermilled rice, that their consumption of rice as a staple be limited to not more than twenty ounces per diem for an average adult, and that a sufficiency of more nourishing foods, especially protein foods, be supplied to them.

Treatment.—The patient should be kept in bed, with good ventilation and a nourishing diet. Diuretics are indicated in most cases, and those should be given which are at the same time cardiac stimulants, digitalis, strophanthus, or diuretin. In other respects the treatment should be symptomatic and expectant.

J. F. Leys.

References.

1. Lancet, Oct. 3, 1908.
2. First Review Trop. Med., Gordon Lab. Khartoum, 1909.
3. Manual of Tropical Medicine, London and New York, 1910.

Berkeley Springs.—Morgan County, West Virginia.

Post-office.—Berkeley Springs. Hotel: Washington.

Access.—Viâ Baltimore and Ohio Railroad to Hancock Station; thence direct to springs. Four trains each way make daily connection at Hancock Station with all day trains on the Baltimore & Ohio R. R. The location is six miles southwest of Potomac River and Hancock Station.

These historic old springs are situated in a narrow valley, about eight hundred feet above the sea level, and issue from the base of a steep ridge rising at this point about four hundred and fifty feet above the valley. Tradition has it that the waters here were well known to the aborigines, who, although generally at war among themselves, established a standing truce around the springs, that all might avail themselves of their potent virtues. They have been known and used by the whites since 1730, and it is said they were visited by George Washington while employed with a surveying expedition in 1748. The Father of his country was so appreciative of the many attractions of the neighborhood that he afterward acquired property immediately adjacent to the principal spring, on which he erected two "comfortable and convenient houses." General Horatio Gates, Charles Carroll of Carrollton, and other well-known figures of Revolutionary days were also represented among the owners in the old town established in 1776. The location of Berkeley is in a beautiful mountain region, covered for the most part by primeval forests, with a botanical undergrowth peculiarly rich, varied, and interesting. The scenery is wild and romantic, and the country is threaded with pleasant walks and drives in all directions. The air is pure and wholesome, and the heat during the summer months is rarely oppressive. The streams in the neighborhood are well stocked with fine game-fish, chief among them being the black bass. The forests also abound in the larger game, including deer, wild turkeys, and pheasants, which afford good sport after September 1. The spacious hotel at Berkeley, has recently changed hands, and has been entirely renovated and refitted. Water from the spring is supplied to each floor. All varieties of hot, warm, and cold baths are at hand, and two large plunge and swimming pools have been constructed. The springs discharge from five principal sources, all within a radius of one hundred yards. The water is clear and sparking and tastless. Its temperature is 74.8° F., which does not vary, and the flow is about 120,000 gallons per hour. The following analysis was

made by C. D. Howard, West Virginia Agricultural Experiment Station:

One U. S. Gallon Contains

Solids	Grains
Sodium chloride	0.14
Sodium sulphate	0.60
Sodium nitrate	0.03
Potassium sulphate	0.12
Calcium sulphate	0.57
Ferrous carbonate	0.01
Calcium carbonate	6.72
Magnesium carbonate	1.11
Strontium carbonate	Trace.
Alumina	0.05
Silica	0.50
Organic matter	0.28
Total	10.13

Gases, Cubic Inches per Gallon.

Free carbonic acid	2.22
Carbonic acid in bicarbonates	7.14
Dissolved oxygen	0.41

Temperature 74.8 degrees Fahrenheit.

The water is evidently of the light saline-calcic variety. The baths at Berkeley have been celebrated for many years in the treatment of gout, sciatica, and rheumatism. The internal use of the water is said to produce excellent results in chronic dyspepsia and diarrhea. Many Virginia families take their children to this resort on account of its reputation as a restorer in rachitis and general feebleness and on account of its value in summer complaints during the period of dentition. The baths possess a marked cosmetic effect, rendering the skin soft, fresh, and elastic, and aiding in the removal of tan and freckles. There are also in close proximity two strong chalybeate springs and a sulphur spring.

Emma E. Walker.

Berkshire Hills.—The Berkshire Hills are situated in Berkshire County, which forms the western extremity of Massachusetts, and are noted for the beauty of the scenery and the healthfulness of their climate, which is a cool and moderately dry one.

This hill country, which is about fifty miles from North to South and about fifteen or twenty miles from east to west, is bounded on the east by the Hoosac Mountains, which vary in height between 1,200 and 1,600 feet; and on the west by the Taconic Mountains, the highest peak of which is Graylock, which is about 3,500 feet above the sea level.

The summer climate of this region is cool, and at all seasons it is free from the harsh, damp winds of the Coast. It is also free from malaria. The winter is decidedly cold, but the air is dry, crisp, and stimulating, and the snow, which is generally abundant, contributes still further to the purity of the atmosphere. In the autumn months this region is, perhaps, at its best, when the air is cool and invigorating and the scenery, with the variegated hues of the changing foliage, is one of rare beauty. "No part of the world possesses a more enchanting summer and autumn than Berkshire."

The average temperature for the four seasons of the year is: Spring, 41.77° F.; summer, 66.2° F; winter, 22.85° F.; autumn, 46.15° F. The temperature has been as high as 97° F. in the summer and as low as —30° in winter at Williamstown, but these extremes, of course, are rare exceptions. The average annual rainfall at Williamstown, which probably indicates about that of the whole region, is 40.58 inches.

Lenox, Stockbridge, Lee, Pittsfield, and Williamstown, the latter the seat of Williams College, are very attractive towns and are favorite and fashionable resorts, with many handsome and attractive homes, a considerable number of which are occupied throughout the entire year. There are delightful excursions all about, and the roads are good for motoring and driving.

This region is a very healthy one, as might be inferred from what has been said. The mortality from tuberculosis, for example, among the inhabitants is more than fifty per cent. below the average for the State.

Therapeutically the climate of this region is favorable for the open-air treatment of tuberculosis, and, in a measure, is comparable with that of Rutland, in the center of the State, where is situated the Massachusetts State Sanatorium; and with the Adirondack and White Mountain regions. "For children the air is extremely favorable," says Dr. J. F. A. Adams of Pittsfield, "cholera infantum being rarely seen, and other summer diseases are comparatively mild." "The dry atmosphere also tends," says Dr. Adams, "to the prevention of rheumatism which is very prevalent along the seaboard." It is also to be recommended for those suffering a breakdown from overwork, for functional nervous diseases, hay fever, and convalescence from acute diseases. On account of its moderate elevation, it is not contraindicated for cases of heart disease or hemorrhage in tuberculosis. (Weber & Hinsdale: Climatology and Health Resorts.)

"Over and above its beautiful scenery, its pure air and generally healthful climate, that particular region is superior to most similar sections of the United States in that it presents throughout the year the attractions of good social advantages, a good percentage of its residential population being persons of cultivation and refinement."

Edward O. Otis.

Bermuda.—The Bermuda Islands lie about 600 miles east of the North American coast about on a line with Charleston, S. C., upon a coral reef which rises from the bed of the Atlantic Ocean. The entire group comprises no less than 365 islands, but, with the exception of some twelve or fifteen, they are far too small to be suitable for human habitation, and of these twelve or fifteen inhabited islands, only five or six are of any considerable size. The largest island of the group is that of Great Bermuda, also called Long Island, which has a length of about sixteen miles, is but one mile and a half broad, and has an area of nine and a quarter square miles. When it is taken into account that the whole group of the Bermudas is comprised between Lat. 32° 14′ and Lat. 32° 25′ N., and between 64° 38′ and 64° 52′ W. Long., occupying, therefore, a portion of the earth's surface only 11′ long by 14′ wide, it is easy to understand how closely packed and crowded together these 365 islands and islets must be. The coral reef underlying this little archipelago, and of which its cluster of islands forms merely the most prominent portions jutting out above the surface the ocean, extends on the western side for a distance of about ten miles beyond the limits of the islands themselves, and it may well be understood that the navigation of these coasts, and the approach to Bermuda are extremely dangerous to ships, and that the services of skilled pilots are always required by vessels entering or leaving their harbors. Nevertheless, the art of scientific engineering has so far overcome these natural obstacles that the island was for many years, one of the chief naval stations in the British empire, to which the Bermuda Islands belong. At Ireland Island, at the entrance of Hamilton harbor, is one of the largest floating docks in the world, and Hamilton harbor itself, although by no means so large as that of St. George's, is nevertheless navigable to large ocean steamships.

The porous limestone rock, underlying the thin

layer of surface soil which covers the islands, rapidly absorbs all the water which falls upon them from the clouds, so that no marshes are to be found anywhere throughout the extent of the Bermudas. Streams of running water and wells are equally absent, and rain water alone constitutes the supply for drinking and for washing purposes. This water is stored in large tanks, each house having one, and no new house is allowed to be occupied until the sanitary inspector is satisfied that the tank has been constructed as directed by law.

The character of the soil is especially suited to the construction of good roadways, hard and smooth, and delightful drives abound in every direction; cycling is also a favorite amusement, and the roads are excellent for this form of outdoor exercise; fortunately the automobile has not as yet invaded these islands. The facilities for fishing and yachting are also unsurpassed.

The following table, condensed from an article in the *British Medical Journal*, 1897, ii., p. 1233, upon "Bermuda as a Health Resort" by E. Harvey, M. D., gives the meteorological data:

Climate of Bermuda—Latitude, 32° 17′ N.; Longitude 67° 47′ W. Period of Observation, January 1, 1893, to December 31, 1896. Elevation of Place of Observation, 150 Feet. (*Fahrenheit Scale.*)

	Average mean temperature deduced from three daily observations.	Average maximum temperature per period.	Average minimum temperature per period.	Mean monthly range of temperature per period.	Mean relative humidity. Per cent.	Average number of fair days.	Average number of clear days.	Average number of fair and clear days.	Average rainfall. Inches.	Prevailing direction of the wind.	Average velocity of wind in miles per hour.
January	62.5°	67.0°	57.5°	9.5°	76	18	2	20	6.25	N.W.	10.8
February	62.2	66.4	56.9	9.5	78	19	3	22	3.98	N.W.	1.8
March	63.9	67.8	56.8	10.0	80	21	3	24	6.53	N.W.	10.2
April	66.1	69.4	59.2	10.2	79	24	2	26	3.08	S.W.	7.9
May	71.4	76.0	64.0	12.0	82	21	2	23	4.86	S.W.	7.2
June	77.7	80.9	70.0	10.9	82	22	3	25	5.59	S.	6.9
July	79.8	84.5	73.1	10.4	83	25	2	27	5.10	S. and S.W.	6.8
August	81.0	85.6	74.0	11.6	81	22	3	25	4.23	S. and S.W.	5.0
September	78.0	83.2	72.3	10.9	80	23	3	26	7.11	S.	5.9
October	73.7	77.5	69.3	8.2	80	23	2	25	6.07	N.E.	8.7
November	68.6	73.5	65.3	8.2	81	19	1	20	3.89	N.E.	9.1
December	64.8	69.0	60.8	8.2	81	18	1	19	5.84	N	11.0
Spring	67.1				80	66	7	73	14.47	N. and S.W.	8.4
Summer	79.5				82	69	8	77	14.92	S. and S.W.	6.2
Autumn	73.4				80	65	6	71	17.07	S. and N.E.	7.9
Winter	63.2				78	55	6	61	16.08	N.W. and N.	7.2
Year	70.8				80	255	27	282	62.54	S. and S.W.	8.4

From the above table it will be seen that the mean temperature for the year is 70.8° F.; for the winter 63.2°, and for the spring 67.1° F. The four months of December, January, February, and March have a mean monthly temperature not varying more than one or two degrees for the several months. The average mean yearly range of temperature is 10° F. The relative humidity is high, the annual mean being eighty per cent. and of the winter seventy-eight per cent. The average rainfall for the year is 62.54 inches. The prevailing winds are from the south and southwest, and, from the personal experience of the writer, are frequent and high.

The average number of fair days in the year is 255, being about the same for each month. The average number of fair and clear days is 282—considerably over two-thirds. The winter and early spring are the seasons of resort to the islands; the summer being extremely debilitating. The characteristics of the climate, then, are mildness, equability, a high degree of moisture, a pure atmosphere free from malaria and fogs, and a large number of fair and clear days.

Although, with the exception of the very damp and warm period, comprised chiefly within the two months of August and September, the degree of elevation attained by the thermometer in Bermuda may indicate a moderate summer temperature, and although the combined features of its climate may indeed render the place an agreeable residence for many persons during the warmer portion of the year, nevertheless, in view of its great humidity, the summer climate can hardly be considered desirable for, and is little likely to be sought by, invalids dwelling in the United States. To many such persons, on the other hand, its mildness and its comparative equability may well recommend the climate of these islands for residence during the whole or during a portion of the winter and spring seasons. There is little doubt that to all persons coming to Bermuda from the severely cold and very changeable winter weather of the Northern United States, the weather of the "Isles of Summer" would appear by comparison delightfully warm and very free from sudden changes of temperature; nevertheless, lest too great and too absolute a standard of equability should be expected by such would-be refugees from our own inclement winter weather, it may be well to remind them that Bermuda is extra- and not intratropical.

Bermuda is connected by cable with Halifax, Nova Scotia, from which it is some 700 miles distant. The time of passage from New York, which is also about 700 miles distant from the island, is now only two days or less and can be made in large and luxurious steamers, which on account of their size largely obviate sea-sickness which was formerly the *bête noir* of a trip to Bermuda in the smaller steamers. The population of Bermuda, in 1896, was 16,000, a large majority of which are negroes. The vegetation is of a semi-tropical character, and very luxuriant. In the season one sees everywhere the white lily fields perfuming the air with their fragrance. The oleander bush grows also in great profusion, and is used for hedges; the banana, guava, pomegranate, avocado pear, tamarind, arrowroot, and many other semi-tropical fruits are found here. The onion, potato, and lily bulb are the principal products exported. In the private gardens many tropical fruits are also found. The houses are all built from the coral rock, and are likely to be damp. The accommodations are good, especially at Hamilton, the principal town of the island and the

place generally selected by the visitor for his residence. Here there are several large well-appointed hotels and many boarding-houses. Thanks to the presence, during the winter months, of the British North Atlantic fleet in the harbor, and of the garrison on shore, there is no lack of social attractions, and Bermuda has become a fashionable winter resort largely due to the excellence of transportation service. The beautiful coral sea gardens, where one sees this curious product in an infinite variety of shapes and colors; the innumerable excursions by sea and by land; the dingey boat sailing; the golf, the bathing, and the fishing; the bicycling and the yachting—all these things afford an abundance of entertainment and outdoor exercise. There is no rainy season, and hardly ever an entirely wet day. The rain quickly soaks through the porous coral soil. The inhabitants spend the greater part of their life in the open air.

In conclusion it is to be emphatically stated that Bermuda is not the sort of place to which patients suffering from phthisis should be sent, although occasionally an individual case, as the writer has known, may do well. Nor is to be selected for cases of chlorosis, general anemia, functional debility, angina pectoris, or palpitation associated with chlorosis. "The class of invalids most benefited by this climate are those in want of mental or bodily rest, or those who should spend most of their time in the open air; cases of mental disease with excitement; the neuralgic, hysterical, hypochondriacal; those addicted to the opium habit, and those who are sufferers from insomnia, nephritis or from chronic disease of brain or cord" (Harvey: *loc. cit.*). To the overworked professional or business man of our northern cities, Bermuda is a veritable paradise.

EDWARD O. OTIS.

Bernard, Claude.—Born in 1813 in Villefranche, near Lyons, France. After making a vain attempt to support himself by literary work he decided, upon the advice of some friends, to adopt the career of medicine. This proved, however, to be a slow affair, and it was only in 1843 that he finally succeeded in obtaining the degree of Doctor of Medicine. Enemy of everything like charlatanism and most conscientious in carrying out his scientific investigations, he met only with failure in his efforts to secure, by competitive examination, the position of assistant professor in the Medical Faculty of Paris; for, at that period, a flowery style of lecturing, without much regard to the real value of the subject matter, counted for everything. Greatly discouraged and lacking sufficient funds for continuing his scientific researches, Bernard had just about made up his mind to settle down in some French village as an ordinary practitioner, when he had the good fortune to contract a marriage with a wealthy heiress. This event made it possible for him to resume his scientific work with a mind free from financial worries. Magendie, who was at this time Professor of Physiology in the College of France, made him one of his assistants, and thus opened the way for him to become at an early day one of the most celebrated vivisectionist investigators in European countries outside France; for, in the latter country, owing to petty intrigues, he continued for a long time to be almost unknown. In 1853 he was elected Professor of General Physiology in the Sorbonne; and, upon the death of Magendie, he was chosen his successor in the College of France. His death occurred on Feb. 10, 1878.

FIG. 639. Claude Bernard.

Claude Bernard ranks as one of the most prominent physiologists of modern times. Personally he was a man of the most genial manners. Of his published writings the following are the most widely known: "Leçons sur la physiologie et la pathologie du système nerveux," Paris, 1858; "Leçons sur la physiologie expérimentale appliquée à la médecine," Paris, 1856; "Sur les propriétés des tissus vivants," Paris, 1866; Sur la chaleur animale," Paris, 1876; and "Leçons sur les phénomènes de la vie," Paris, 1878. The following may be ranked as the most important of the discoveries made by Claude Bernard: the fact that the cervical sympathetic nerve possesses vasomotor functions; the fact that the chorda tympani nerve possesses secretory functions; and the fact that pricking the floor of the fourth ventricle of the brain causes sugar to appear in the urine.

A. H. B.

Bernays, Augustus Charles.—Born at Highland, Madison County, Illinois, on Oct. 13, 1854. He studied medicine at the University of Heidelberg, Germany, at first under Friedrich Arnold and Gegenbaur, both of them celebrated anatomists, and afterward under Gustav Simon, the surgeon. He received the doctor's degree in July, 1876, after passing the required examinations with the highest credit (*summa cum laude*). From Heidelberg he went to Berlin and took a special course under B. Langenbeck, the celebrated surgeon of that city. Subsequently he visited Vienna and took a similar course under Billroth. Early in 1878 he established himself in practice in St. Louis, Missouri; and in the course of about two years he had already made such headway that he did not hesitate to confine himself, from that time forward, to purely surgical work, that branch of medical science in which he took the greatest interest and in which he felt confident that he could gain the greatest success. His subsequent career revealed clearly the wisdom of the course which he adopted. The triumphs which he won in abdominal surgery, and more particularly in the surgery of the stomach, and the skill which he manifested in plastic operative work, justify us in placing him well in the front rank of American surgeons. He died in May, 1906.

FIG. 640.—Augustus Charles Bernays.

Dr. Bernays made numerous contributions to medical literature. Only a few of these, however, may be enumerated in this brief sketch. They bear the following titles: "Cancer of Superior Maxilla, etc.," in *St. Louis Medical and Surgical Journal*, xxxiv., 1878; "Oesophageal Abscess," *ibidem*, xxxvi., 1879; "Amputation without Ligatures," *ibidem*, xxxviii., 1880; "Spontaneous Gangrene of the Penis in an Old Gentleman about Sixty Years of Age," *ibid.*, xlv., 1883; "A Successful Case of Total Extirpation of the Uterus through the Vagina," *ibid.*, xlvi., 1884; "A Case of Cystic Tumor in the Jaw of a Negro," etc., in the *Medical Record*, xxviii., 1, 1885; "On the Relations between Cells and Microorganisms,"

in *Journal of the American Med. Association*, vi., 4, 1886; "Gastrotomy for the Removal of a Swallowed Knife," etc., in *St. Louis Med. and Surg. Jour.*, lii., 9, 1887; and "Three Cases of Total Excision of the Cancerous Tongue, *ibid.*, liii., 333, 1887.

A. H. B.

Bert, Paul.—Born at Auxerre, France, in 1830. While he was traveling in Algiers, before he had any intention of adopting medicine as a vocation, he noticed that the zouaves, on several occasions, and simply as a matter of sport, cut off a rat's tail, made a wound somewhere along the animal's back, and then transplanted the amputated part to this newly made opening. After the tail had healed in its new position Bert discovered that it retained its sensibility, and he thus became interested to learn along what route the nervous impulses were conducted. Upon his return to Paris he began the study of natural history, and utilized the experience narrated above as the theme for the dissertation which he wrote when he made application for the degree of Doctor of Medicine (1863). In 1868 he was made one of Claude Bernard's assistants; and when the latter resigned the Chair of Physiology in the Sorbonne and attached himself to the Museum of Natural History, Bert delivered a few lectures, first in the Sorbonne and then in the Museum. These lectures were published in Paris, in 1868, under the title: "Leçons sur la physiologie comparée de la respiration." During the Franco-Prussian War he was appointed Prefect of the *Département du Nord*, and after the termination of the war he was elected Professor of Physiology in the Sorbonne; but he was never given an opportunity to show what his capabilities were as a teacher, for, having been chosen as a Deputy, to represent his native city in the legislature, the laws of France would not permit him to continue lecturing while he held this political office. Then, early in 1886, he was sent to Tonkin, China, in the character of "General-Resident," but, on the eleventh day of November of the same year, he died of tropical dysentery.

His most important published writing is that entitled: "La pression barométrique, etc.," Paris, 1878.

A. H. B.

Bertillon System.—See *Anthropometry*.

Betaine Hydrochloride.—This is the salt, $C_5H_{12}NO_2Cl$, of betaine (trimethylglycocoll) which is found in the beet and other plants. It is made synthetically by the action of monochloracetic acid on trimethylamine. It is used in some gastric affections marked by deficiency of hydrochloric acid, on the ground that the drug liberates that acid in the stomach. The dose is one to five grains (0.06 to 0.30). It is soluble in water, slightly so in alcohol, and insoluble in chloroform or ether. It is sold under the trade name of *Acidol*.

R. J. E. Scott.

Betanaphthol.—By the substitution, in the molecule of the hydrocarbon *naphthalene*, of an hydroxyl group (—OH) for one of the atoms of hydrogen, a derivative, $C_{10}H_7.OH$, is obtained, bearing precisely the same relation to naphthalene that common phenol (carbolic acid) does to benzene. Such derivative is styled *naphthol*, and according to the position of the hydroxyl substitution, two distinct naphthols are obtainable, known respectively as *α-naphthol* and *β-naphthol*. In the alphanaphthols the OH replaces H in one of the positions nearest the fusion of the two rings; in betanaphthol the OH replaces H in one of the positions furthest removed from the fusion of the two rings. Of these two bodies *β-naphthol* is the more easily made, is the less toxic, and is the article used in medicine. It is official in the United States Pharmacopœia under the title and spelling Betanaphthol; in the Pharmacopœia of 1890 it was called Naphtol.

Properly purified, betanaphthol presents itself in beautiful silver crystalline scales, nearly or entirely odorless, but of a sharp, burning taste. The crystals are very slightly soluble in water (in about 1,000 parts of cold, and in seventy-five parts of boiling water), but dissolve freely in boiling alcohol; betanaphthol is also soluble in ether, chloroform, and solutions of the alkali hydroxides. Gently heated, it sublimes, and may be distilled with steam. It should be kept in dark amber-colored bottles, well stoppered. Betanaphthol is locally distinctly irritant, exciting upon tender surfaces redness, smarting, and even inflammation, and, upon the healthy skin also, if in *alcoholic* solution, acting occasionally with sufficient energy to develop an eruption resembling nettle-rash. Solutions in oils or fats, however, are said to be without effect upon the sound skin, although acting energetically upon an eczematous surface (Kaposi).

Constitutionally, betanaphthol, in therapeutic doses, produces but little derangement. Some experimental dosings of animals have been followed by hemoglobinuria, with convulsions and death, and, in one instance in the human subject, an external application of betanaphthol produced hematuria, ischuria, unconsciousness, and eclampsia (Kaposi). But since these effects are exceptional, it is likely that the samples used in the cases cited were not pure. Ordinarily doses of from 0.20 to 0.32 grams (gr. iij. to v.), given a number of times daily, are innocent of harm beyond some possible disturbance of the stomach. The medicine therefore ranks among the non-poisonous, and its value lies in the fact that while it is thus non-poisonous to the human system it is yet quite potent to arrest the development of many micro-organisms. It is said to be five times as powerful in this regard as carbolic acid; at the same time it is less toxic than phenol. Betanaphthol is accordingly used as an internal medicine to disinfect the alimentary canal, as in cases of diarrhea, dysentery, intestinal dyspepsia, and especially in typhoid fever, in which disease its efficacy was first proclaimed by Bouchard. The doses are those already mentioned, and it is usually administered in a capsule or cachet. The article is also used as a local application in many skin diseases, notably scabies, psoriasis, and eczema. It is commonly applied in ointment ranging in strength of betanaphthol from one-half to ten per cent., or even fifteen per cent. The remedy should not be used upon denuded parts, and weak applications only should be made to irritated parts such as so commonly present themselves in eczema.

R. J. E. Scott.

Betanaphthol Benzoate—($C_6H_5CO_2.C_{10}H_7$). Obtained by the reaction that takes place between betanaphthol and benzoyl chloride. It is a whitish, crystalline powder, without taste or odor, very slightly soluble in water, freely soluble in chloroform and alcohol. It is also called benzonaphthol.

It is recommended as a substitute for salol or betol, having the advantages that benzoic acid possesses over carbolic or salicylic acid. It is not acted upon in the stomach, but in the small intestine it breaks up into betanaphthol and benzoic acid.

The former is not absorbed and remains in the intestines until excreted; the latter also exerts a local antiseptic action, but ultimately is absorbed and eliminated with the urine. It is incompatible with antipyrine, camphor, phenol, menthol, potassium permanganate, and urethane.

This is one of the newer intestinal antiseptics that have secured a favorable recognition. It has proved of value in ordinary fermentative changes in the intestine, and in the diarrheas of children and adults,

both acute and chronic. In an epidemic of acute dysentery in Cuba it proved of marked value, the death rate in those cases in which it was employed being only two per cent., while under other methods of treatment it was nine per cent.

The ordinary dose is from three to eight grains (0.2–0.5) three or four times a day, but when a more decided action is desired a larger dose must be administered—up to a maximum of thirty grains (2.0) a day to children and sixty grains (4.0) to adults. It is best prescribed in capsules or cachets, with a little charcoal. No ill effects have been reported from the employment of this remedy. BEAUMONT SMALL.

Betel Nut.—See *Areca*.

Bethlehem, N. H.—This summer resort in the White Mountains can be taken as a type of the many others in this region which are visited by thousands of persons on account of the cool, pure mountain air and attractive scenery. This region is also famous for the exemption from hay fever enjoyed here, and Bethlehem, of all the other resorts, has the greatest reputation in this respect.

It is picturesquely situated on the western slope of the mountains, seventeen miles west of Mt. Washington. It is 1,459 feet above sea-level, and is only exceeded by Dublin in the southwestern part of the State, which has an elevation of from 1,500 to 1,600 feet.

From the situation of Bethlehem on the west of the mountain range, the air is dryer than that on the eastern side; for the humidity from the Atlantic Ocean is deposited on the eastern slope, and, in consequence, the air reaches Bethlehem freed from much of its moisture. Another reason for the dryer atmosphere is the absence of any large bodies of water in this vicinity.

The town itself is situated on a sort of table-land overlooking, toward the north, the valley of the Ammonoosic. It is protected from the east winds by Mt. Washington and other mountains of the Presidential Range, and also, in the near vicinity, by Mt. Agassiz and a high hill. Toward the west there are hills and valleys, and in this direction one obtains a view of the distant Green Mountains of Vermont. It is open toward the south.

There are an efficient system of sewerage and a pure water supply. The accommodations are ample and good, from well-equipped hotel to the more modest boarding house. At Maplewood, a mile away, formerly a part of Bethlehem, now an independent township, there is the extensive caravansary, the Maplewood Hotel. There are excellent golf links and a casino. Many and varied excursions can be easily made from this center and the roads are generally good for motoring. For one who is exiled here on account of hay fever, a more charming refuge can hardly be imagined.

The season is a long one, extending late into September. Indeed, the early autumn days are most delightful, when the forests are brilliant with the changing foliage, and the air is crisp and invigorating.

The climate in summer is characterized by purity of air, coolness (although there is a hot day occasionally), equability, a comparative low relative humidity, usually a small amount of rain, and a comparative absence of easterly winds. The mean temperature of the months of July and August and the first two weeks in September, as observed by Dr. W. H. Geddings, for nine years, is as follows: July, 66.04° F.; August, 65.34° F.; September, 63.36° F. For the same periods, with the addition of one more week in September, as observed by Dr. C. F. McGahan, for seven years, we have: July, 67.7° F.; August, 62.9° F.; September, 61.8° F. The mean temperature of the nine seasons observed by Dr. Geddings was 64.91° F.; and of the seven years observed by Dr. McGahan, 64.1° F. The daily range of temperature for a period of two years (according to Geddings) was 10.3° for July and August. The relative humidity for five seasons (Geddings) was 65.5 per cent.

The prevailing wind is southwest, and there are a large number of clear days. The average for July and August (Dr. McGahan, seven years) being 23, and out of 21 days in September 17 were clear.

Hay fever is the disease which has made Bethlehem famous on account of the immunity from it which one enjoys here and there is no place in the United States where one can more surely obtain relief from this distressing affliction. The Hay Fever Association of the United States holds its annual meeting here and its members declare that more of them are exempted from this disease at Bethlehem than at any other place.

Other conditions benefited by this climate are asthma, the ally of hay fever; convalescence from long and exhausting diseases; exhaustion from care, worry, and overwork; malnutrition in children; the weakness and depression resulting from influenza; and such other conditions as require a pure, cool, stimulating mountain air.

For pulmonary tuberculosis this is an excellent climate, comparable to that of the medium altitudes, such as the resorts in the Adirondacks, Berkshires, and elsewhere. There is no reason why the cure could not be continued the year through here. Indeed, the best results, as we know, are obtained in the colder months of the year, and a continuous treatment under careful supervision without change of locality for summer and winter is generally to be advised.

There are many other well-known resorts in the White Mountains, all possessing similar climatic characteristics, modified by the local conditions of their situation. Such are: Jefferson, Randolph, Crawfords, Twin Mountain, Dixville Notch, and Bretton Woods, where is the very large and luxurious Mt. Washington Hotel, with extensive grounds carefully kept, golf links, and many delightful walks and excursions. Nearby one takes the train for the ascent of Mt. Washington.

By a recent law much of the White Mountain region will eventually become a national reservation, thus preserving the forests and woodlands which remain, much of which, unfortunately, has already fallen under the woodman's axe.

EDWARD O. OTIS.

Betol.—Betanaphthol salicylate, naphthosalol, $C_6H_4.OH.COO.C_{10}H_7$, the betanaphthol ether of salicylic acid, analogous to salol which is the phenyl ether of salicylic acid. It occurs as an odorless and tasteless, white, shining, crystalline powder, insoluble in water but readily soluble in warm alcohol. It passes unchanged through the stomach, but in the alkaline fluids of the intestine it is split up into betanaphthol and salicylic acid. Its therapeutic action is similar to that of salol (phenylis salicylas, U. S. P.). It is employed in the treatment of rheumatism, gonorrheal and other forms of cystitis, and as an intestinal antiseptic in typhoid fever and the summer diarrhea of infants. Dose, gr. v.–viii. (0.3–0.5) in capsules or emulsion, or mixed with milk. R. J. E. SCOTT.

Betony.—*Wood betony, Stachys betonica* Benth (fam. *Labiatæ* is a perennial herb of Europe, growing in pastures and woods. The leaves, when fresh, have a faint, disagreeable odor—which mostly disappears upon drying—and a bitter astringent and nauseous taste.

Betony in former times had a high reputation for a variety of troubles; at present it is not in use. Dose of

the dried leaves as a "nervine, expectorant, sudorific," etc., is from one to three grams (gr. xv. to xlv.). The root is said to be emetic. H. H. Rusby.

Bex.—A climatic resort in the Canton of Vaud, Switzerland, containing also saline springs which are employed for baths and douches. This little town of about 4,500 inhabitants is beautifully situated in the valley of the Rhone, sixty-eight miles by rail from Geneva, and eleven miles from the Lake of Geneva. It is 1,427 feet above sea-level. The narrow valley, on the right side of which lies Bex, is shut in on either side by lofty mountains, and between them rushes the Rhone on its way to Lake Geneva. In the immediate vicinity of Bex the valley and mountain sides are well wooded, and there are many beautiful walks, long or short, as well as more arduous mountain excursions. Bex, from its situation in a valley, is free from wind.

The season in which Bex is at its best and is most visited is in the spring, particularly May and June. In the autumn patients frequent the place for the grape cure, for which it is famous.

The mean annual temperature is about 50° F. During the shortest days of winter the sun shines but a few hours.

The saline springs are nothing but strong brine waters obtained from the distant salt mines and conveyed to the bathing establishments. The principal ingredients in 10,000 parts are given as follows:

Chloride of sodium	1,567.0
Chloride of potassium	26.5
Chloride of magnesium	10.8
Sulphate of lime	67.6

Ten to twenty quarts of this brine are used to a bath. Diluted and charged with carbonic acid gas, it is used internally.

The Nauheim baths are also given here. The hydrotherapeutic establishments are well equipped with inhalation cabinets, sprays, douches, etc. The diseases and conditions which are benefited by these baths, and the climate as well, are delicate children and those with glandular or bone tuberculosis; chronic catarrhal affections; subacute rheumatism; certain uterine affections, such as metritis, subinvolution, etc.; asthma; anemia; the milder forms of neurasthenia; and certain cases of paralysis following infectious diseases. Cases of nephritis, especially with edema, should avoid saline waters, for recent investigations have shown that salt and chloride retention is dangerous in this disease; hence, in the treatment of nephritis, waters devoid of salt are to be chosen.

The accommodations are excellent. The Grand Hotel des Salines is situated about three-quarters of a mile from the village in a fine park, and is equipped with hydrotherapeutic apparatus. In the village are other good hotels and pensions, all moderate in price. There are an English-speaking physician, and an English Church.

Besides the grape cure which has been mentioned, the milk and whey cure is also carried out here. The quality of grapes used in this "cure" is said to be excellent. Edward O. Otis.

Biarritz.—A seacoast town in the extreme southwestern portion of France (lat. 43° 29′ N.), a short distance from Bayonne and not far from the boundary between France and Spain. This resort has a commanding situation on a high plateau or rocky headland, descending quite abruptly to the sea (the Bay of Biscay). The beach is smooth and sandy, with a good surf, which is often high. "There is no sightseeing in Biarritz save the sea, its sunsets, cliffs, and beach."

Biarritz has become a well-known fashionable seaside resort, and is frequented by visitors from all parts of France, Spain, and other countries during the bathing season, which not only comprises the summer months but extends much later into the autumn than is the case with similar seaside stations lying farther to the north. It is also a winter resort, being especially favored by the English at this season.

The accommodations are excellent and abundant, and although it is rather an expensive resort in the summer, the winter rates are more moderate. The sanitation and drainage are good and in every respect Biarritz affords all the conveniences and luxuries of a fashionable watering place. There are English physicians, Protestant churches, clubs, casino, and golf links.

It is hot in summer, but the sea breezes temper the heat. In winter the temperature is mild and comparatively equable. At this season the climate is "agreeable and healthy," very similar to that of Arcachon.

A particularly important characteristic of such a seaside resort situated so far south, is that one can enjoy essentially the same conditions of climate and bathing in the autumn which exist on the more northerly coast only in the summer months. In some respects Biarritz resembles the resorts on the English Channel, but it is far inferior to the Riviera or the east coast of Spain.

The mean winter temperature (according to Weber) is from 42.8° F. to 46.4° F.; the mean spring temperature, 51.8° to 53.6° F.; and that of the summer about 64.4° F. The relative humidity is given by Weber as about eighty per cent. and the annual rainfall 49.21 inches. The rain is quickly absorbed by the sandy soil. During the winter the climate is comparatively mild, bracing, and sunny, and a considerable amount of time can be spent in the open air.

The prevailing wind is the northwest from the ocean, which is violent at times. The south wind (Solano) is dry and hot, but does not last long.

The class of patients likely to be benefited by a stay at Biarritz during the winter months are such as, not seriously ill, require a moderately mild, sunny, invigorating climate, amid cheerful surroundings, and whose condition is not aggravated by the large amount of moisture and the winds. Such are cases of neurasthenia and nervous depression, dyspepsia, chlorosis, and cachectic conditions. For diseases of the respiratory tract, such as pulmonary tuberculosis and chronic catarrhal conditions, it is too windy, for it lacks the protection from the winds which Arcachon, not far distant, enjoys on account of its situation in the pines some miles from the Atlantic coast.

The bathing is excellent and there are swimming pools or baths cut in the rocks. There is also nearby a large and fully equipped hydrotherapeutic establishment where brine baths are given for the usual maladies for which such baths are applicable.

There are various amusements afforded: golf, tennis, a casino with music, regattas, etc. The walks and excursions are varied and interesting. One can easily cross into Spain from here. Besides the "excellent hotel accommodations Biarritz abounds in comfortable and attractive villas, often surrounded by gardens, and situated at various points close to or even directly upon its picturesquely rocky shores."

Edward O. Otis.

Bibiru Bark.—*Greenheart Bark, Nectandræ Cortex.* The bark of *Nectandra rodiæi* Schomb. (fam. *Laura-*

ceæ). This is a fine forest tree of British Guiana, where it is highly prized as a source of the best ship timber.

The bark is now rarely imported, in large, long, heavy, flat pieces, from 0.5 to 1 centimeter in thickness (one-fifth to two-fifths inch). It is hard and brittle, breaking with a coarse, fibrous fracture; it is grayish brown externally, cinnamon brown and striated upon its inner surface. Its cells are seen under the microscope to be thickened, those of the liber curiously dentated. It has a strong bitter taste, *without aroma*—an unusual thing for any member of its family.

The bitterness of this substance is due principally to the alkaloid *buxine* (bibirine, bebeerine—not berberine), which it contains to the extent of one-half or one per cent. It also contains *nectandrine* and one or two other alkaloids, and tannin. The seeds are sometimes made use of as a source of starch.

The bark, and especially the alkaloid and its salts, have been offered, and to some extent employed as a febrifuge and antiperiodic, that is, as a substitute for quinine; but in reasonable doses they fall far short of that medicine for the purpose. They are, however, good simple bitter tonics (the bark is astringent as well). Doses: a useful dose of the bark would be large and disagreeable. Buxine or its salts may be given, as a tonic, in pills or solution, up to gr. iii.–vi. (0.2 to 0.4); as a febrifuge, up to gr. xv.–xxx. (1.0–2.0). H. H. Rusby.

Bichat, Marie-François-Xavier.—Born Nov. 11, 1771, in Thoirette, France. He began his medical studies in Lyons, in 1791 or 1792. At first, he devoted his attention exclusively to anatomy and surgery; but, in the latter part of 1793, owing to the disturbed state of politics in that city, he went to Paris and followed very closely the clinics of Desault, the celebrated French surgeon. At that period of his life his only ambition was to become skilled as a surgeon, in order that he might serve in this capacity in the army. Between 1795, when the death of Desault occurred, and 1802, when Bichat met with the accident which terminated his life in the course of a fortnight, the latter accomplished more than most industrious men are able to accomplish in a score of years. He completed (1795) the fourth volume of the "Journal de Chirurgie de Desault"; edited the "Oeuvres chirurgicales de Desault," in three volumes (Paris, 1798–1799); and wrote and published a book entitled "Traité des membranes" (Paris, 1800), another entitled "Les Recherches physiologiques sur la vie et la mort" (Paris, 1800), a third on general anatomy (Paris, 1801), and a fourth on descriptive anatomy (Paris, 1801–1803). And while he was doing this prodigious amount of literary work he attended almost daily to his duties as a hospital physician, responded to the numerous calls made upon his time and strength by his private patients, performed over six hundred autopsies, and lectured to the students of the University. The natural result of this "burning the candle at both ends" was that Bichat's strength, shortly before his death, was almost completely exhausted; and one day, while he was descending one of the stone staircases of Hôtel-Dieu, he fell and probably struck upon his head. Fourteen days later (July 22, 1802) he died.

Fig. 641.—Marie-François-Xavier Bichat.

Bichat was not only a man of great intellectual capacity, he also possessed traits of character that endeared him to all who came in contact with him; he was modest, perfectly frank, kindly, and of a generous disposition. A. H. B.

Bienaise, Jean.—Native of Mézières, France, in which town he was born about the year 1601. Dezeimeris (Dict. Hist. de la Méd.) says that he was one of the boldest and yet at the same time most skilful operators of the seventeenth century. Called in consultation to see Anne of Austria, widow of Louis XIII. of France, who was affected with cancer of the breast, he did not hesitate to proclaim to her boldly that all the promises of a cure which the charlatans of that day had made to her, were purely vanity, and that some measure of alleviation was all that his art could procure for her disease. For a period of two years he accompanied Louis XIV. in his campaigns in Flanders, and was shown by this monarch that he valued his services highly. He died on December 21, 1681, at the age of eighty.

A few years after the death of Bienaise the only treatise which he had ever written was published. Its title reads as follows: "Les opérations de la chirurgie, par une méthod courte et facile, avec deux traités," Paris, 1688, and another edition in 1693. The two supplementary treatises mentioned in this title have reference to "the nature and cause of diseases of the stomach" and to "venereal diseases." In the main work will be found an account of the "concealed or covered bistouri" which probably suggested to Frère Cosme (see under the heading: *Baseilhac, Jean*) the idea of his "concealed lithotome." Bienaise used this covered bistouri in operating upon cases of fistula in ano. A. H. B.

Bier's Method.—See *Hyperemia, Therapeutic.*

Biermer, Anton.—Born in Bamberg, Germany, Oct. 18, 1827. He received the degree of Doctor of Medicine in 1851. After acting in the capacity of an Instructor (Privatdozent) in Internal Diseases, in the University of Würzburg, for several years, he accepted successive calls to the regular chair of this branch of medicine in the following Universities: Berne, Switzerland, in 1861; Zürich, Switzerland, in 1867; and Breslau, Germany, in 1874. He held the latter position up to 1891, when the condition of his health obliged him to resign. His death occurred on June 24, 1892.

Biermer ranks as one of the most distinguished clinicians of modern times. Specially noteworthy are the investigations which he made with regard to sputa and also with regard to asthma. His method of rendering the ciliary movement easily visible in the mucous membrane of a tracheotomized animal is still to-day the method most commonly employed for this purpose. The following are among his most important published writings: "Ueber die Richtung und Wirkung der Flimmerbewegung auf der Respirationsschleimhaut des Menschen, Kaninchens und Hundes," 1851; "Die Lehre vom Auswurf," 1855; and "Ueber Asthma bronchiale und über Entstehung des Typhus abdominalis," in Volkmann's Sammklinische lung Vorträge. A. H. B.

Bigelow, Henry Jacob.—Born in Boston, Massachusetts, in 1818. He received the degree of Doctor of Medicine from the Harvard Medical School in 1841. In 1845 he began teaching surgery in the Tremont Street Medical School, and in 1849 he was appointed Professor of Surgery in the Harvard Medical College,

a position which he held until 1886, a period of thirty-seven years. In 1846 he was elected a member of the surgical staff of the Massachusetts General Hospital. In 1878 Bigelow introduced the operation of litholapaxy, or lithotrity with complete evacuation of the fragments of the stone at one sitting. The method was received by surgeons with instant favor and soon supplanted the old operation of lithotrity and also in great measure lithotomy. His death occurred on Oct. 30, 1890.

Bigelow's "Manual of Orthopedic Surgery" was awarded the Boylston Prize in 1844. Of his later

Fig. 642.—Henry Jacob Bigelow.

published writings the following deserve to receive special mention: "Ununited Fracture successfully treated, with Remarks on the Operation," Boston, 1867; "The Mechanism of Dislocation and Fracture of the Hip, with the Reduction of the Dislocation by the Flexion Method," Philadelphia, 1869; and "Litholapaxy or Rapid Lithotrity with Evacuation," Boston, 1879. A. H. B.

Bigelow, Jacob.—A distinguished medical practitioner, botanist, teacher, and writer; was born in Sudbury, Mass., on February 27, 1787. He was graduated from Harvard University in 1806, and commenced the practice of medicine in Boston in 1810. He early became known as a skilful botanist, having an extensive correspondence with botanists in Europe, and several plants were named for him by Sir J. E. Smith in England, by Schrader in Germany, and in France by De Candolle. In 1814 he published "Florula Bostoniensis," and in 1815 "American Medical Botany," in three volumes, illustrated by colored plates after nature. At this period he occupied the chair of Materia Medica in Harvard Medical College, and also that of Clinical Medicine; he was an active practitioner in Boston for forty years, enjoying a large and lucrative practice; also for a long period physician to the Massachusetts General Hospital. From 1816 to 1827 he delivered lectures on "Application of Science to the Useful Arts," which resulted in the establishment of the Massachusetts Institute of Technology.

In 1820 he was one of the Committee of Five selected to form the American Pharmacopœia; and the nomenclature of the Materia Medica, substituting (when practicable) a single for a double word, is due in principle to him. He also published numerous medical essays and discourses, some of which are to be found in a volume entitled "Nature in Disease." One of these, "Discourse on Self-limited Diseases," had great influence in modifying the practice of physicians at that time in regard to the treatment of acute diseases. In 1854 he was elected Corresponding Fellow of the New York Academy of Medicine. He died in Boston on January 10, 1879.

Bigelow was the founder of Mount Auburn Cemetery in Boston. The stone tower, chapel, gates, and fence were designed by him, and the colossal Sphinx, in granite, was a gift from him. For many years he was President of the Massachusetts Medical Society, and of the American Society of Arts and Sciences. In 1856 the trustees of the Massachusetts General Hospital placed his bust, in marble, in their hall, in commemoration of his long-continued services.

T. L. S.

Bile.—Bile may be obtained for examination either from the gall-bladders of men or animals after death, or from biliary fistulæ. The principal methods of establishing fistulæ in animals for experimental purposes are briefly as follows:

Permanent Fistulæ.—An incision is made over the gall-bladder. Through this the common bile-duct is tied in two places and a portion excised between the ligatures. The gall-bladder is then sewed to the sides of the abdominal wound and opened.

Amphibolic Fistulæ.—The gall-bladder is brought to the surface and opened as in the preceding method, but the bile-duct is left intact. This method has an advantage over the other inasmuch as the external opening may be plugged and the bile allowed to follow its usual channels into the duodenum, or it may be left open, when the bile will flow externally, and, if not allowed to discharge for too long a time, will be more normal in character.

Temporary Fistulæ.—The common bile-duct is exposed and opened, a glass cannula is tied in, and the bile is drawn off through a rubber tube attached.

Quantity of Bile Secreted.—The amount obtained through fistulæ is very variable in different animals, both absolutely and in proportion to the body weight. The rate of flow varies much in the same animal from hour to hour. In human subjects with biliary fistulæ the daily discharge has usually been between 400 and 900 c.c., and the total amount of solids between five and twenty grams.

Physical Properties.—Human bile as obtained from the gall-bladder is usually of a yellowish or reddish-brown color, but when exposed to the air may become green by oxidation of bilirubin to biliverdin. Its reaction is faintly alkaline. The specific gravity varies from 1.005 to 1.010 or over in fistula bile, but is much higher in bile taken from the gall-bladder after death, frequently reaching 1.030, or even 1.050. It has a bitter taste with a suggestion of sweet. Human bile has little or no smell; that of the ox and sheep has a faint musk-like odor. As secreted by the liver cells bile is non-viscous; but, during its stay in the ducts and gall-bladder, it has added to it the secretions of their mucous membranes, containing mucin (human), or nucleo-albumin (ox), and it acquires a certain viscidity. On spectroscopic examination it may be seen to absorb the violet and some of the blue rays, but shows no definite absorption bands unless postmortem changes have occurred.

Chemical Composition.—The principal constituents of bile are as follows: water, bile salts, bile pigments, mucin, fats and soaps, cholesterin, lecithin, urea (traces), and inorganic salts. Among the salts the most important are the chlorides of sodium and potassium, the phosphates of calcium, magnesium, and iron, and traces of manganese, copper and zinc. The quantities of these constituents vary considerably, but the analyses contained in the following tables may be taken as fair examples of a great number which have been published:

In 1,000 parts of bile.	Human gall-bladder bile. Frerichs. Man of 22 killed by violence.	Human fistula bile. Hammersten. One of three published in Hammersten's "Physiological Chemistry."
Water	859.2	974.6
Solids	140.8	25.4
Bile salts	91.4	9.04
Glycocholate		6.86
Taurocholate		2.18
Mucin and pigments	29.8	5.15
Fat	9.2	.61
Fatty acids from soaps		1.01
Cholesterin	2.6	1.5
Lecithin		.65
Inorganic substance	7.7	7.46

The *bile salts* are the most abundant of the solid constituents and give to the bile its most important properties. The commonest bile salts, and those which have been most studied, are *sodium glycocholate* ($C_{26}H_{42}NaNO_6$), and *sodium taurocholate* ($C_{26}H_{44}NaNSO_7$), the former being most abundant in herbivorous animals and man, and the latter in carnivorous animals. The bile salts are soluble in water and alcohol, but insoluble in ether. If bile be mixed with freshly heated animal charcoal and evaporated to dryness, the bile salts may be dissolved out with absolute alcohol along with several other biliary constituents. If an excess of ether be now added, the bile salts alone are precipitated, forming "*Plattner's crystallized bile.*" Under the microscope this may be seen to consist of bell-shaped masses, star-like clusters of fine needles, or four to six sided prisms. Both the bile salts and their acids are dextrorotatory to polarized light.

Sodium glycocholate	(a) D = +25.7°
Glycocholic acid	(a) D = +29.0°
Sodium taurocholate	(a) D = +24.5°
Taurocholic acid	(a) D = +25.0°

In the intestines, the respective acids are set free from the bile salts and then further broken up into a complex non-nitrogenous acid, cholalic acid, and either glycocoll or taurine.

Glycocoll, glycocine, glycine, or amino-acetic acid (NH_2CH_2COOH) is one of the products of the splitting up of sodium glycocholate. It is found free in the intestines in small quantities, and may combine in the body with benzoic acid to form hippuric acid, in which form some of it may leave the body by the urine, especially in the case of herbivorous animals. Glycocoll may be formed from the decomposition of proteins, and is in some cases a precursor of urea. It is probable, however, that glycocoll, taurine, and cholalic acid, when set free in the intestine from the decomposition of the bile salts, are reabsorbed, and combined once more in the liver to form a new supply of bile salts. This cycle of events is known as the "*circulation of the bile salts.*"

Taurine, amino-isothionic acid, or amino-ethylsulphonic acid ($NH_2.C_2H_4.SO_2.OH$), is obtained from sodium taurocholate. Like glycocol it is formed from the decomposition of proteins, but differs from it in containing sulphur. It is also found free in the intestines in small quantities.

Cholalic, or *cholic acid* ($C_{24}H_{40}O_5$), is set free, as stated above, when either sodium glycocholate or sodium taurocholate is split up, and it is found in the intestinal contents. Certain closely allied acids may replace it in the bile salts, among which the most important are *choleic acid* ($C_{24}H_{40}O_4$) and *fellic acid* ($C_{23}H_{40}O_4$), both of which have been obtained from human bile.

On the presence of cholalic acid depends Pettenkofer's well-known test for bile salts and bile acids.

Pettenkofer's test for bile acids is performed as follows: A small quantity of the solution to be tested, freed from proteins, is placed in a test-tube, and two or three drops of a ten-per-cent. solution of cane sugar are added, and the whole shaken. Strong pure sulphuric acid is then added drop by drop, care being taken that the temperature of the mixture does not rise above 70° C. If bile acids are present the fluid first becomes opalescent, then the opalescence clears, and the liquid becomes successively of a pale cherry red, a dark carmine red, and finally a beautiful purple violet tint. The reaction sometimes takes a little time to develop, and it is wise to wait several minutes before drawing a negative conclusion. To make the test perfectly reliable, the colored solution obtained must be examined by the spectroscope, when two absorption bands will be found, one at F, and the other between D and E, near E. This is rendered necessary by the fact that a number of other substances, among which are proteins, oleic acid, amyl alcohol, morphine, and numerous aromatic substances, give a similar color reaction, but may be distinguished by causing different absorption bands.

The Bile Pigments.—The pigments constantly found in human bile are bilirubin and biliverdin.

Bilirubin ($C_{16}H_{18}N_2O_3$) occurs in the bile of all vertebrates, but is most abundant in that of carnivora and man, giving it its yellowish or reddish-brown color. It may be obtained as an amorphous powder, and also as reddish-yellow rhombic plates. It is readily soluble in chloroform, less so in alcohol, and still less so in ether. It is insoluble in water, and exists in bile as a soluble calcium compound, known as bilirubin-calcium. It forms a considerable part of some gallstones, and is present in the blood serum of certain animals (horse), in old blood extravasations, and in the tissues and urine in cases of jaundice. It is identical with hematoidin, an iron-free derivative of hemoglobin; it owes its origin to broken down red corpuscles and is probably the principal source of the stercobilin of the feces and of the urobilin of the urine. Under the influence of oxidizing agents bilirubin is converted into biliverdin.

Biliverdin ($C_{16}H_{18}N_2O_4$) is present in all green-colored biles, among which are to be included those of the herbivora and some examples of human. When obtained pure, it usually consists of a dark green amorphous powder, but occasionally crystallizes in green rhombic plates. It is insoluble in water, ether, and chloroform, but soluble in alcohol, glacial acetic acid, and strong sulphuric acid. It is converted by reducing agents into bilirubin, and this change often occurs in the human gall-bladder, which explains the fact that bile obtained from that source after death is nearly always of a reddish-brown color, while fresh fistula bile is occasionally green.

Hydrobilirubin ($C_{32}H_{40}N_4O_7$), a reduction product of bilirubin, may be formed from it in the laboratory, and is regarded by some as supplying a link between the pigments of bile and those of the feces and urine.

Tests for Bile Pigments.—Gmellin's Test. Spread out a few drops of the suspected liquid on a white plate. Let a drop of fuming nitric acid (containing nitrous acid) fall in the center. If bile pigments be present a ring of colors, green, blue, violet red, and yellow, will appear. This is due to the oxidation of the pigments, by which bilirubin is changed successively into biliverdin (green), bilicyanin (blue), bilipurpurin (violet red), and choletelin (yellow). The blue pigment bilicyanin, in acid solution, gives a spectrum with two absorption bands, one on either side of the D line, which fuse into one if the solution be very strong. The yellow choletelin gives a single band between b and F, nearer to F.

Huppert's Test for bilirubin. Add to the suspected liquid milk of lime till a precipitate (bilirubin-calcium) is thrown down. After washing this precipitate in water, place it in a test-tube, and half fill the test-tube with alcohol acidified with hydrochloric or sulphuric acid. Boil for some time, and if the original liquid contained bilirubin, an emerald green or bluish-green color will develop.

Mucin.—As already mentioned, the mucin present in human bile is largely derived from the secretions of the bile-ducts and gall-bladder. In many animals it is replaced by nucleo-albumin. These substances resemble each other in their viscidity, and are both readily precipitated from bile by acetic acid, but differ in the products of their decomposition. Mucin splits up into a protein and a carbohydrate; nucleo-albumin, on the contrary, into a protein and a complex nitrogenous substance, rich in phosphorus, known as nucleic acid.

Fats.—These consist principally of palmitin, stearin, and olein, with the corresponding soaps.

Cholesterin ($C_{27}H_{45}OH$), is a complex monatomic alcohol. It is present in nearly all animal tissues, especially those of the central nervous system. It is insoluble in water, but freely soluble in ether, chloroform, and hot alcohol. It crystallizes out from alcoholic solutions in colorless transparent plates. From anhydrous ether or chloroform it separates in the form of needles.

Lecithin ($C_{42}H_{84}NPO_9$) is found along with cholesterin in nearly all animal tissues. It yields on decomposition glycerin, a fatty acid, phosphoric acid, and an alkaloid known as choline.

Action of Bile.—Bile is partly an excretion, and partly a secretion playing a part in digestion and absorption. Its digestive properties depend almost entirely on the presence of the bile salts. In some animals traces of diastatic ferment have been found, but never in sufficient amount to play any important part in digestion. The principal action of bile is on the fats, and depends on the fact that solutions of the bile salts have the power of dissolving free fatty acids. The present tendency is to the view that fats are absorbed as fatty acids and soaps, in solution, rather than in the form of emulsion. If this be so, the part played by the bile is very important. After the neutral fats are split up by the pancreatic juice into glycerin and fatty acids, the latter are dissolved by the bile and partly converted into soap by its alkaline salts. Moreover, bile is able to dissolve the soaps of the alkaline earths (calcium) which would otherwise be insoluble. There is an old view, that the bile also exerts a favorable influence on the absorptive functions of the intestinal wall; this may depend partly on its power of dissolving fats and partly on its property of diminishing surface tension.

The function ascribed to it of preventing putrefaction in the intestine is to be explained by its aiding fat digestion so that the fatty food is absorbed before it has had time to undergo putrefactive change. Then it must be remembered that the absorption of the fatty portions of the food will expose the other constituents better to the action of the pancreatic juice, so that all the digestive processes will proceed more rapidly. It is claimed by T. R. Fraser that the bile has antitoxic powers by which it is able to antagonize and render inert powerful organic poisons like those of snake venom.

There is satisfactory experimental proof that the several ferments of the pancreatic juice are most active in the presence of bile, although just how it favors their action is not fully explained. The bile also serves a useful purpose by precipitating the undigested proteins and the pepsin as they enter the intestine from the stomach. The precipitate is redissolved by the alkaline juices of the intestine but the activity of the pepsin is destroyed so that it cannot have the destructive action on the pancreatic ferments which it otherwise would.

The bile salts are extremely irritating to the pancreas and some cases of pancreatitis are caused by the bile finding its way back along the pancreatic duct as a result of obstruction at the mouth of the common bile duct. The mucin of the bile is protective and if present in large quantities protects the pancreas to some extent from the action of the bile salts.

Biliary concretions or gallstones may be divided into two principal types:

1. Dark-colored, hard, non-inflammable stones, consisting principally of calcium compounds of the bile pigments (especially bilirubin-calcium) and calcium carbonate.

2. Lighter-colored soft stones, which will melt and burn in a flame, and consist very largely of cholesterin.

Other constituents often found in gallstones are: bile acids, free bilirubin, phosphates of lime and magnesium, sulphate of lime, sodium, potassium, copper, manganese, silicic acid, mucin, and epithelium. Most gallstones are intermediate in composition and properties between the two extreme types given above, and vary in color from nearly white, through golden or greenish yellow, to reddish brown and black. Many stones vary in color and composition in different layers.

Among possible causes which have been suggested for gallstones the following may be mentioned:

1. Excess of lime and deficiency of sodium salts in the bile, leading to precipitation of the pigments.

2. Presence of chronic catarrh, leading to excessive secretion of mucin.

3. Excess of cholesterin in the blood as a result of excessive brain work, old age, or other causes.

4. Concentration of the bile from stagnation.

5. Naunyn's theory, which now receives much support, combines several of the above, and may be briefly stated thus:

Gallstones are the result of a pathological alteration in the mucous membrane of the gall-bladder, usually excited by the presence of microbes, and leading to an increased excretion of lime and cholesterin.

T. Wesley Mills,
William S. Morrow.

Bile Passages.—See *Gall-bladder* and *Liver.*

Bilharz, Theodor.—Born in Sigmaringen, Germany, on March 23, 1825. He received the degree of Doctor of Medicine, in 1849, from the University of Tübingen. In the same year he accompanied Prof. Griesinger to Egypt, in the capacity of Assistant of the Medical Clinic. Remaining in Egypt after Griesinger's return to Germany, he was eventually (1855) appointed Professor of the Medical Clinic in the Kasr-el-Aïn school in Cairo. His death occurred on May 9, 1862.

Bilharz owes his reputation in part to the investigations which he made in association with Prof. Griesinger, and to a still greater degree to the fact that he discovered the Egyptian entozoön which bears his name—*Hæmatobium bilharzii.* A. H. B.

Bilharzia.—*Schistosoma.* A genus of trematode worms. *B. hæmatobium* causes hematuria in parts of Africa and Asia. A male and female are always found fastened together. These parasites are found in the blood-vessels which they often rupture and may cause serious trouble in the urinary bladder or other parts of the body. See *Trematoda.* A. S. P.

Biliousness.—The older descriptions of biliousness include anorexia, furred tongue, constipation, headache, more or less vertigo, nausea, etc., occasionally slight jaundice, and vomiting of bile-stained stomach contents. By the laity the term is often used as a euphemism for constipation or sometimes for diarrhea.

Biliousness was formerly considered a definite perversion of function—supersecretion of bile, however much the symptoms might differ. Others have considered it the expression of hepatic congestion—without necessarily denying the excess of secretory or excretory function. Another view has been that, instead of a supersecretion, there was a deficient excretion of bile, with resulting cholemia.

Most modern authors have dropped the term altogether or retain it as a matter of convenience. Most cases corresponding to the clinical picture of biliousness present two main conditions: marked reduction or even absence of free HCl in the stomach, with more or less obvious fermentation; intestinal putrefaction with indol in the feces and indican in the urine. There may be true gastric or intestinal catarrh, the latter more often a colitis, perhaps localized as a typhlitis or even more definitely in the appendix.

It must be admitted that there are certain important relations of the factors found in "biliousness" to hepatic and biliary disease.

1. If gastroenteritis precedes and causes the secretory conditions mentioned, the former is very likely to be due to hepatic sclerosis producing back pressure in the portal circulation.

2. Conversely, there is both clinical evidence that repeated attacks of indigestion, with products of fermentation and putrefaction passing to the liver, are a marked cause of hepatic sclerosis; and feeding experiments with indol have produced hepatic sclerosis.

3. A very plausible argument may be made connecting either active or passive congestion of the liver with certain of the suppositious conditions and described symptoms of "biliousness."

4. Bacterial activity in the intestine, especially involving increased virulence or functional activity of the colon bacillus, is very apt to lead to invasion of the gallbladder and is one of the recognized causes of calculi.

5. Moreover, such bacterial activity, while undoubtedly explaining what has loosely been termed intestinal indigestion, is by some authorities, regarded as depending in large measure upon true indigestion. An important item in the latter is failure of biliary secretion. Indeed, while the simplest experiment proves that bile is not an antiseptic and that it will itself putrefy, there is almost unanimous agreement among physiologists and clinicians that free secretion of bile is an important indirect factor in preventing an excess of bacterial activity in the intestine.

6. Without accepting the older conception of biliousness or of the cholagogue action of various drugs, it is well established that certain ingredients of bile, especially the taurocholate and glycocholate of sodium, primarily secretions, are reabsorbed from the intestine and again excreted. Apparently, toxic substances are absorbed along with these and the cathartic action of certain drugs removes the old stock of biliary salts, indirectly compels fresh secretory activity, possibly along other lines than the mere formation of these ingredients, and also eliminates intestinal toxins.

In the immediate treatment of biliousness, especially when gastric fermentation, nausea, and headache are conspicuous, aromatic spirit of ammonia or a solution of sodium bicarbonate gives relief. A purge, usually of calomel or other mercurial followed by a saline, is routine treatment. Lavage of stomach or colon may be indicated but is usually considered disproportionate to the condition. If gastric lavage is practised, it may be followed by the writer's method of spraying a five per cent. solution of menthol in pure petrol (pure mineral oil) which is immediately sedative and indirectly stimulant of secretion. If there seems to be need of stimulating the liver, very hot water should be used in the lavage and about a quart left in the stomach or the patient may drink very hot water to the amount of a couple of liters in two or three hours. In either case, sodium chloride, ammonium chloride, or the mixed blood salts may be added to make a physiological solution. Hydrotherapy of this nature washes not only the stomach and upper part of the intestine but, through portal absorption, the liver as well, and produces marked diuresis, clearing up slight jaundice and removing indications of toxemia.

Subsequent treatment includes attention to diet, which should be simple but of fair variety and well balanced, except that there is usually an indication for a low meat and fat constituent. There is no general objection to fresh vegetables, fruits, or even sugar. Dilute hydrochloric acid, best given about one hour after meals, in empirical dose of 1 c.c. (♏ xv.) or, as determined by titration, to bring the stomach contents to an acidity of 2 : 1000, is both a digestant and an antiseptic and also seems to act as a stimulant to the liver.

Buttermilk or a lactic acid culture is indicated if there is putrefaction with indol formation, contraindicated if there is much carbohydrate fermentation or fat rancidity. While it is fashionable to sneer at intestinal antiseptics, phenol salicylate or the safer acetyl salicylate, menthol, acetozone, and many other compounds seem to mitigate the virulence of bacterial action in the intestine. Magnesium peroxide and the peroxoles are highly praised by some. Animal charcoal, thoroughly dry, absorbs toxins and gases, as does the old fashioned remedy, bolus alba. The salicylates also come somewhere near the requirements of a cholagogue and are prophylactic of calculi even if not of some value in causing their softening and disintegration. No attempt will be made to discuss the treatment of underlying conditions. A. L. Benedict.

Billings, John Shaw.—Born in Switzerland County, Ind., April 12, 1839. After graduation from the Medical College of Ohio, Cincinnati, in 1860 he was appointed demonstrator of anatomy in this institution. Two years later he was commissioned assistant surgeon in the U. S. Army. At the close of the Civil War he was placed in charge of the library of the Surgeon-General's office in Washington, and in 1883 was appointed Curator of the Medical Museum and Library. In 1894 he was made Lieutenant-Colonel and Deputy Surgeon-General. He was retired with the rank of Lieutenant-Colonel in 1895. While in charge of the Medical Museum and Library he began the publication of the "Index Catalogue," and started, with the cooperation of Dr. Robert Fletcher, the *Index Medicus*, a natural outgrowth and complement of this great catalogue. He was also the moving spirit in the planning and organization of the Johns Hopkins Hospital, Baltimore. In 1896 he was appointed Director of the New York Public Library and was in charge of this institution during its period of formation by the consolidation of the Astor, Lenox, and Tilden foundations, being credited with the whole plan and arrangements of the new central library building. He was a member of many medical and other scientific societies in this country and abroad. He died March 11, 1913.

Among Dr. Billings' most important contributions to medical literature may be mentioned "Principles of Ventilation and Heating," 1886; "The National Medical Dictionary," 1889; and the "Index Catalogue of the Library of the Surgeon-General's Office," 16 volumes, 1880–1894, the latter remaining as a tribute to his genius for organization and to his bibliographical attainments. T. L. S.

Billroth, Christian Albert Theodor.—Born in Rügen, a Prussian island in the Baltic Sea, on April 26, 1829. He received the degree of Doctor of Medicine from the University of Berlin, in 1852. From 1853 to 1860 he was an assistant in B. von Langenbeck's Surgical Clinic in Berlin. In 1860 he received the double appointment of regular professor of surgery and director of the surgical clinic in the University of Zürich, Switzerland. He

remained in Zurich up to 1867, when he was given the corresponding positions in the University of Vienna, Austria. In 1870 he gave his professional aid to the Germans in the Franco-Prussian War. In the spring of 1887 he fell seriously ill for the first time in his life and the attack left him with a permanently crippled heart, which finally caused his death on February 6, 1894.

FIG. 643.—Christian Albert Theodor Billroth.

Billroth—to quote the words of his biographer in Pagel's "Biographisches Lexikon"—was justly considered a star of the first magnitude in the surgical firmament. A large part of his reputation may properly be attributed to what he accomplished in abdominal surgery, a new field of work that had been brought into existence by the discovery of antiseptic and aseptic procedures. In addition to his successes in abdominal surgery he should be credited with the first complete extirpation of the larynx (1874) and the first successful resection of the pylorus (1881). Finally, his lectures on General Surgical Pathology and Therapeutics furnished delight an valuable instruction to many generations of students. A. H. B.

Binet, Alfred.—Born in Nice, France, July 8, 1857. About 1880, after completing the regular course of medical studies, Binet decided definitely on a psychological career. In 1892 he became associated with Prof. Beaunis in the direction of the laboratory of physiological psychology at the Sorbonne; and in 1895, on the retirement of Prof. Beaunis, he was given sole charge of the laboratory. He died on October 18, 1911.

Binet ranked as one of the foremost psychologists of France. He was a prolific writer, and, among the numerous books which he published, the following may be enumerated as showing the varied character of his work: "La psychologie du raisonnement, etc"; "La perception extérieure"; "Psychologie des grands calculateurs et joueurs d'échecs"; "La suggestibilité"; "Les idées sur les enfants." He is the author of what is known as the Binet-Simon test of mental capacity in children. A. H. B.

Binet-Simon Tests.—See *Intelligence, Tests of.*

Binucleata.—A group established by Hartmann, to include the *Hæmosporidia* and the binucleated flagellates, which has not been generally accepted by protozoologists. See *Protozoa.* A. S. P.

Biogenesis.—*Recapitulation Theory.* The principle that ontogeny repeats phylogeny, or that the stages through which every individual animal passes in its development represent in general the past history or evolution of the race to which it belongs. A. S. P.

Biology.—(βίος, life, and λόγος, a discourse.) *Definition.*—"The subjects of our inquiry will be the various forms and phenomena of life, the conditions and laws under which this state occurs, and the causes through which it is brought about. The science that occupies itself with these subjects we will designate by the name *biology*, or the science of life." This, in translation, is the definition of biology given by Treviranus in 1802, and it applies equally well to-day.

The term has not always been used with this meaning, however. The Oxford Dictionary gives three ways in which it has been employed.

(1) It was used in England for the first time by J. Stanfield ("Biography," 1813, p. 12), in its true etymological meaning to designate "the study of human life and character," as distinguished from biography, the history of the lives of individual men.

(2) The unfamiliarity rather than the etymology of the word probably accounts for a use that appears to have arisen in this country. The writer has heard it stated by the late president of the Johns Hopkins University that when it was proposed to establish there a biological laboratory in 1876 the name "biological" was regarded with suspicion as suggestive of the fakir. This was because, as stated by W. B. Carpenter ("Principles of Mental Physiology," 1870, p. 550): "About the year 1850 'the world was turned upside down' by a couple of itinerant Americans, who styled themselves 'professors' of a new art which they termed *electrobiology;* asserting that, by an influence of which the secret was known only to themselves, but which was partly derived from a little disc of zinc and copper held in the hand of the 'subject' and steadily gazed on by him (whence the designation which they adopted), they could subjugate the most determined will, paralyze the strongest muscles, pervert the evidence of the senses," etc. "Electrobiology, or *'biology'* (as it came to be very commonly designated) was not merely introduced at scientific reunions, but became a fashionable amusement in some circles, at ordinary evening parties, and thus it happened that a large proportion of the public became familiarized with the phenomena." Professed "biologists" gave public exhibitions, and Carpenter himself speaks of "the biologized subject" and of "biological phenomena," meaning thereby what we now understand by hypnotism.

(3) Fortunately that use of the word has become obsolete, and biology is employed at the present time in both popular and scientific language with the meaning originally given to the word by Treviranus in the passage quoted at the beginning of this article.

HISTORY OF BIOLOGY.—Biology is relatively a new science. The famous Roman naturalist Pliny embraced within his "Natural History" all realms of nature, including man and his activities. But as the result of the theological ideas of the Middle Ages, man became to be regarded as something apart from nature. Thus Lord Bacon ("Advancement of Learning," 1605), divides the descriptive sciences into history of nature and history of man, and the knowledge of causes into divine philosophy, natural philosophy, and human philosophy; but all divisions of knowledge, he said, are like the branches of a tree that meet in a stem.

Gradually as the mass of human knowledge grew and was more classified, various branches were split off from natural history, such as astronomy and physics, which, because they dealt more with the causes than with the descriptions of phenomena, were called natural philosophy, using Bacon's term in a somewhat different sense. Later chemistry emancipated from the mysticism of alchemy, became a distinct science, and the name natural history was restricted to the sciences that appeared to be purely observational.

Buffon, writing in the middle of the eighteenth century, divided all science into civil history and natural history. But his natural history was essentially descriptive and was divided into three sections dealing with animals, plants, and minerals. He recognized, however, a unity in nature so that one may descend by nearly insensible degrees from the most highly organized animal to the simplest mineral; and he

regarded man as the animal which occupies the highest point in his scale.

Bonnet, in his "Contemplation de la nature" (1764), goes one step farther than Buffon by saying, after making an extended comparison, that animals and plants are only modifications of organized matter. He described an animal as an organized being which is nourished by internal roots, and a plant as one in which the roots are placed outside. They are nevertheless essentially the same, he says, and the character by which they may be truly distinguished is unknown to us.

It remained for Bichat, in 1801, to draw a clear distinction between organic and inorganic beings, between physiological and physical sciences. He based his distinction upon the possession, by organic beings, of the properties of irritability and contractility.

In the following year (1802) the term biology was proposed by Treviranus and Lamarck to cover what Bichat called the physiological sciences. Whether the word was coined independently by these two writers as supposed by Geddes, or whether it was borrowed by Lamarck from Treviranus, as stated by Littré, is not important. In any event, the chief credit is due to Treviranus, for he not only invented the name, but he set to work earnestly to erect the science that it was intended to designate, publishing his results in a book of six volumes entitled "Biologie, oder Philosophie der lebenden Natur." But, unfortunately for his success, the foundations upon which he had to build—systematic zoology and botany, morphology, physiology, and general anatomy—were only then being established. Not only were these sciences incomplete as to matter, but, as he says, they were then as isolated as the pyramids in the sands of Egypt. Nevertheless, he succeeded in producing what Huxley has well termed a very remarkable book, one that is essentially modern in its plan and execution; very different from the work of his countryman Oken, which, although more highly regarded at the time, would now be considered medieval rubbish.

Treviranus was seriously hampered in his treatment of the subject by the fact that the two great generalizations which were to furnish the true scientific bases for the unification of the biological sciences had not then been formulated. These were: the cell theory, propounded by Schleiden and Schwann 1838; and the theory of the origin of species by means of natural selection, published by Darwin and Wallace in 1858. Thus it happened that, while the point of view of Treviranus was appreciated and upheld by a few such men as Auguste Comte and Isidor Geoffroy Saint-Hilaire, and was being confirmed, perhaps unconsciously, by the contributions of others, the great majority of zoologists, botanists, anatomists and physiologists failed to look beyond the confines of their special provinces.

By the publication of the "Origin of Species" a new light was thrown upon organic nature which not only showed the essential unity of the animal and vegetable kingdoms, including mankind, but also, by eliminating the supernatural factor, served to bring biology into harmony with the other natural sciences. Under the leadership of Herbert Spencer and Huxley in England and of Haeckel in Germany this new point of view has been widely propagated until now in many colleges and high schools a student may get his first introduction to natural science through a course in general biology.

THE LIVING SUBSTANCE.—Since its publication in 1838 the cell theory has been greatly modified by the researches of Max Schultze and many other investigators. At the present time one of the chief reasons for the union of botany and zoology in a single science called biology is found in one of the generalizations of the cell theory as now accepted—namely, that the physical basis of life, the living substances, or *protoplasm*, has certain fundamental characteristics which are essentially the same wherever it may be found.

(1) *Occurrence.*—In the first place, the living substance always occurs in certain definite aggregates, that we call *organic individuals*. To be sure, many non-living substances may also occur in aggregates with a definite form—that is, in crystals. But the crystal differs from the organic individual in many important particulars. A crystal of sodium chloride may be crushed, or even dissolved, but its substance still remains sodium chloride. On the other hand, a blow on the head is sufficient to convert a living ox into dead beef. As the result of an injury to a part, the whole aggregate has ceased to be living substance and has become a mere mass of proteins, fats, and salts. But what is the difference between the living and the dead ox? Its form and proportions remain the same. It has not lost weight, and we may infer from this that a chemical analysis of the carcass will enable us to ascertain the kind and proportion of the chemical elements that were present in the living body; although we shall still be ignorant as to what rearrangements of these elements may have taken place in the course of death.

(2) *Activities.*—The great difference between the dead and the living, then, is not in form or substance but in activity. If we beat the dead ox, it will not move away; if we place hay and grain in its stomach, it will not be dissolved and converted into ox-stuff. Just as the ox differs from the salt and the beef that I am to have for dinner, so the living oak tree differs from the crystal on the one hand and from the wood of my table on the other. The wood can no longer take in carbon dioxide and oxygen from the air, water and salts from the ground, and convert them into oak-stuff. Neither can it respond to the stimuli of light or gravity. What is true of the ox and the oak is true of animals and plants in general, and thus we find certain powers of activity which they possess in common and which distinguish living beings from all other bodies. These may be summarized as follows:

(*a*) *Assimilation.*—This is defined by Verworn as "the sum of the processes that lead to the construction of living substance to the maximum of its most complex constitution, the synthesis of proteins."

In these processes various non-living substances are brought into contact with the protoplasm and are there converted into living substance like itself.

(*b*) *Dissimilation.*—Hand-in-hand with assimilation goes the reverse process, dissimilation, the giving off of non-living material, waste products, from the living substance. Assimilation and dissimilation, anabolism and catabolism, are two phases of *metabolism*, a process that is continuous in a living organism. Its cessation, however, does not necessarily imply death, for it has been shown that there is no metabolism in seeds that are dried but which are still capable of germination under proper conditions. Moreover, as Verworn has pointed out, the process is not without its analogy in inorganic chemical processes. In the manufacture of sulphuric acid, the nitric acid which is used, or rather the nitroyl-sulphuric acid formed during the reaction, is continually being built up and broken down, so that if fed with a continuous supply of sulphurous anhydride, water, and oxygen a small amount of nitric acid may produce an unlimited quantity of sulphuric acid, without any diminution of its own substance. Similar phenomena may be observed in Deacon's process for the manufacture of chlorine, and in other chemical operations in which catalytic substances are used.

Nevertheless metabolism, and especially its constructive phase, assimilation, is a process that is highly characteristic of a living being, and is not ordinarily met with elsewhere in nature.

(*c*) *Growth.*—Whenever assimilation exceeds dissimilation, increase in size, or growth, of the organism takes place.

(*d*) *Reproduction.*—Growth leads to reproduction, or the separation from the organism of a part of the living substance to form a new organism like the parent.

(*e*) *Irritability.*—This has been defined as "the capacity of a body to react to an external influence by some kind of change in its condition, in which the extent of the reaction stands in no definite proportion to the extent of the influence." This highly characteristic property is possessed by all living substances. It finds its analogy, however, in certain non-living substances, the explosives. But there is one difference between the explosion of an unstable chemical compound and the reaction of an organism to a stimulus. The explosion results in the destruction of the mass, while an organic reaction is normally purposeful in character and tends to the preservation of the mass.

(3) *Structure.*—While it is possible to find some analogy between the activities of protoplasm and other processes in nature, there are certain minute structural features to be found in substance that is living, or has lived, for which we may look elsewhere in vain. The fundamental generalization of the cell theory is that every animal or plant is a cell, or a collection of cells and their products. A cell may be defined as a mass of protoplasm with its contained nucleus. It is found by experiment that if a portion of the protoplasm be separated from the nucleus, it may still respond to stimuli, but it can no longer assimilate food or repair damage. It has lost the power to perform some of the essential vital functions. Likewise a nucleus deprived of its surrounding protoplasm, or cytoplasm, is incapable of continuing life. Thus we are led to regard the cell as the unit organism, and its structure as a fundamental characteristic of the living substance.

As to the ultimate structure of protoplasm, there has been great diversity of opinion. The best view appears to be the one that in its simplest form the structure of the protoplasm is like that of an emulsion, in which the continuous substance is the active living material, and the inclusions, ranging in size from the largest yolk granules to bodies at the limit of microscopic vision, are passive materials in various stages of metabolism. But, superimposed upon this vesicular structure, there may be also a fibrillar structure (see *Cell*). It may be noted that while the complex organization of the cell is characteristic of the living substance, the more minute vesicular structure of protoplasm has been shown by Butschli to have an analogy in the structure of certain inorganic colloidal substances.

(4) *Chemical Composition.*—It is in their chemical composition that Verworn finds what he regards as the one fundamental character that all animals and plants have in common and that distinguishes them from all other bodies. This characteristic is the possession of a class of highly complex compounds of nitrogen, carbon, hydrogen, oxygen, and sulphur known as the proteins. Both fats and carbohydrates also occur very generally in animals and plants, and with the proteins form their chief constituents. That all three classes of compounds are found in the living as well as in the dead cell is shown, according to Verworn, by "a careful comparison especially of the solid bodies that may be found as reserve substances for a time unchanged in the living cell, with the corresponding substances of the dead cell." Nevertheless, there are differences between living and dead protoplasm that show that death involves a chemical change. In the first place, living protoplasm usually has an alkaline reaction or is neutral, while dead protoplasm is generally acid. Then there are certain proteins that are fluid in life and coagulated at death. The difference is again shown by the effects of diamide and hydroxylamine. These substances are strong poisons, that is, they destroy living protoplasm, producing presumably substitution products; but they have no effect upon dead protoplasm. Moreover, while alive, protoplasm is continually undergoing change, taking up oxygen and giving off various products of metabolism, but when dead it is stable, and under certain conditions may remain unchanged for years. So while it is true that the three classes of compounds characteristic of dead protoplasm are found also in that which is living, they do not have exactly the same molecular structure. Therefore a chemical analysis of dead protoplasm will not reveal the exact chemical constitution of the living substance.

(5) *Origin.*—Finally the living substance, whether it be animal or vegetable, differs from all other substances in its mode of origin. Other chemical compounds may be formed anywhere that the necessary elements are brought together in favorable combinations and under the right conditions of temperature, solution, etc. We know nothing in regard to the conditions under which living matter was first produced, and we are equally ignorant as to what future discovery may bring forth; all we know at present is that the living substance appears to be peculiar in that the only conditions under which it can be produced are those found in the living organism, animal or plant as the case may be. Lifeless material is converted into living substance only by the process of assimilation. This takes place only in the presence of preexisting living substance. This great generalization, called by Huxley the doctrine of *biogenesis*, is due to the labors of Redi, Pasteur, and their successors; and is the fundamental fact upon which is built the modern practice of aseptic surgery.

Other Points of Agreement between Animals and Plants.—If the fundamental similarities between animals and plants that have just been enumerated are not deemed sufficient to establish the union of the biological sciences, we may seek further into the details of the structure and vital processes in organisms, and there we shall find still more striking evidence of their essential unity.

Not only does the definition of a cell as a mass of protoplasm surrounding a nucleus apply equally well to multicellular animals and plants and to the unicellular organisms, classed by Haeckel together under the name Protista; but we find that certain details of structure are always found in cells wherever they may occur. This applies more especially to the nucleus, which ordinarily in the resting condition is a rounded sac-like body surrounded by a delicate membrane. Enclosed within the membrane is a structure usually described as a reticulum, but more probably an alveolar structure, consisting of two substances, *linin* and *chromatin*, while the spaces within the alveoli or reticulum are filled by a clear *nuclear sap*. Even in bacteria and other microorganisms which do not possess a well-defined nucleus, granules are found scattered about in the cell which shows the same color reactions as chromatin.

Cell division in both animals and plants is always preceded by the division of the nucleus, which usually takes place by what is called the indirect method (*karyokinesis*, or *mitosis*). The essential thing in this method is the exactly equal division of the chromatin (see article *Chromosome*).

In both animals and plants increase in the number of individuals may take place by three methods of reproduction—fission, budding, and sexual reproduction (*gamogenesis*). Sexual reproduction dif-

fers from the other modes in that the new individual arises from a cell that is derived from the union of two cells usually having origins in different individuals (see *Sex*).

In both animals and plants the cells that are to take part in sexual reproduction undergo a preparatory change which results in a reduction in the amount of chromatin; and even in the unicellular organisms in which the sexes are not differentiated a similar process is found to occur (see *Maturation*).

In the union of two cells to form a germ (oöspore) the essential process is the union of the two nuclei. While the details of this process differ in different species, it always results in the formation of a nucleus in which the chromatin is derived from the male and the female parent in exactly equal parts, except for the recently discovered idiochromosomes, which are derived from only one parent, usually the male, and are supposed to contain the factor that determines the sex of the offspring (see *Sex*). In the conjugation of the unicellular organisms, even where there is no union of the cell bodies, there is formed likewise in each individual a new nucleus to which each one has contributed just half of the chromatin (see *Impregnation*).

Differentiation of structure goes hand-in-hand with division of labor. It may occur within a single cell, resulting in the specialization of different parts of the cell to perform different functions; or, in multicellular organisms, it may cause whole cells or large masses of cells to differ from others, forming tissues and organs for various functions. In both animals and plants the causes of differentiation may be divided into two classes. One depends upon the structure or chemical composition of the protoplasm itself, the other depends upon the external conditions surrounding the organism (see *Differentiation*).

In the developing organism differentiation is followed by growth, which takes place according to the same laws in both animals and plants (see *Growth*).

In both animals and plants the offspring tends to resemble its parents at the corresponding stages of growth. This is not merely the result of development under similar external conditions. A change in the environment will result in a change in the organism; but you may change the environment as much as you please and still you cannot cause the egg of a star-fish to develop into a sea urchin, or *vice versa*. Embryos of two species may be reared under perfectly identical conditions, yet each one will come true to its kind. This tendency among organisms for like to produce like, depending upon something in the structure of the germ, is what we mean by *heredity*. The researches of Galton, Pearson, Bateson, and others show that the laws of heredity among animals apply equally well to plants (see *Heredity*).

Finally we are indebted to Charles Darwin for the discovery of the principle of *natural selection*, which is equally applicable to animals and plants as an explanation of the phenomena of diversity, or the origin of species (see *Evolution*).

A measure of the advance made in general biology during the last one hundred and fifty years may be obtained by comparing such a list of the similarities of animals and plants as that given in the preceding paragraphs with the discussion of the same subject to be found in the second part of Bonnet's "Contemplation de la nature," published in Amsterdam in 1764.

Divisions of Biology.—Biology has been divided into subordinate sciences without number. For example, we have carcinology, the study of crabs; conchology, the study of molluscs; mycology, the study of fungi; cytology, the study of cells, gastroenterology, the study of the alimentary tract, etc.—each separate group of organisms or organs having its own special "ology." These subjects may be arranged in groups from several different points of view. The biological sciences may be divided into two great groups, *botany* and *zoology*, dealing respectively with plants and animals. Or we may distinguish between organisms now living and those known only by their fossil remains. Then we have *recent biology* and *paleontology*. Again, from normal biology we may separate the study of the abnormal conditions of organisms, *pathology*. Finally, and this seems to be the best arrangement, we may follow Huxley and divide *biology* into four great groups—*morphology*, *physiology*, *chorology*, and *etiology*. The relations of these sciences, to which we may add *anthropology*, are exhibited in the accompanying scheme (Fig. 644).

Morphology (μορφή, form) is the study of the structure of organisms. It includes *general anatomy*, or *histology*, the study of the microscopic structure of cells, tissues, and organs; *anatomy*, which may be purely descriptive, as human anatomy; or comparative, when it has for its aim the discovery of homologies; *ontogeny*, including embryology, the study of development within the egg, and the study of post-embryonic development and metamorphosis. The facts of anatomy and development form the basis for the classification of organisms, which is treated under *taxonomy*.

Another branch of morphology is *pathological anatomy*, dealing with the histology and gross anatomy of diseased tissues and organs. *Paleontology* includes the morphology of fossil organisms, although this term is generally restricted to the morphology of fossil animals, while paleobotany is used for plants.

Physiology (φύσις, nature), on the other hand, has to do with the functions of organisms, more especially the activities of the cells, tissues, and organs. These may be divided into *generative*, including the phenomena of reproduction; *sustentative*, including digestion, absorption, circulation, and the complex phenomena of metabolism and secretion; *correlative*, including the relations between stimuli and reactions, and the physiology of the muscular and nervous systems. The study of the perturbations of these functions under diseased conditions gives us *pathological physiology*. Partly physiological and partly morphological is the study of the phenomena of growth differentiation, heredity, and variation. These subjects may be classed together as *morphological physiology*, or *experimental morphology*.

Chorology (χώρα, dwelling place, area of distribution) is a term invented by Haeckel to include all the phenomena of distribution of organisms. These may be studied from three points of view, geographical, topographical, and geological, the last giving an account of the succession of forms in geological history.

Etiology (ἀιτιολογία, giving a cause) is a term long used by physicians to designate the study of the causes of disease. Originally, however, it had a broader meaning—the study of causation in general. It is in this sense that Huxley has borrowed the term and used it to designate the group of biological sciences which have for their aim the explanation by general physical laws of the origin and present condition of living beings upon the globe. This includes *ecology* (οἶκος, household), the science dealing with the total relations between organisms and the surrounding outer world; also called bionomics, and including most of what is popularly meant by natural history. The facts of morphology, physiology, and distribution, as well as those of ecology, all contribute to the theories of *evolution*, whereby it is sought to explain the origin of species; and from the study of fossil remains, aided by comparative anatomy and embryology, it is possible to form a conception of the *phylogeny*, or history of the changes which the various groups of animals and plants have undergone in the ages that are past.

Psychology and *sociology* are not usually regarded

as parts of biology, and, as Huxley has remarked, the biologist has already quite enough to do without including these sciences within his field of study. Nevertheless some biologists and many others are now actively engaged in spreading the doctrine that not only are these sciences an integral part of biology, but also their application for the welfare of mankind will be effective just so far as they are based on sound biological principles. The mental activities which form the subject-matter of psychology are after all only certain special functions of the brain, and as such their study becomes only a subdivision of the physiology of the nervous system.

Anthropology embraces the whole range of the biological sciences in their relation to mankind, including certain divisions, however, that apply only to the genus Homo. These divisions relate especially to the human activities that are associated with the advance of civilization. Studies of the past are included under *ethnology* and *history;* the present conditions and relations of mankind are the subject of sociology, which in its pathological aspect becomes *criminology*.

Sociology deals with Man; with the relations of Man to his environment, organic as well as inorganic; and with the interrelations of Man with Man, both male and female. The basis of sociology is man, and the basis of man is his germ-plasm. But the finished product, the adult man or woman, is the product of the germ-plasm formed and moulded by the environment; and one of the most interesting and practically important of the problems of sociology is the determination of the relative value of these two factors. Has nature or nurture a preponderating influence in the development of the individual man? This is one of the questions of the day. Another biological question that is now uppermost in the minds of sociologists, is how may the principles of heredity be applied to maintaining and improving the standards of the human race? To the study of this problem Sir Francis Galton gave the name of *Eugenics*.

The relations of men in a commonwealth do not differ essentially from the relations of bees in a hive, and may equally well be considered the subject of a special branch of ecology. The scientific principles that form the basis of sanitation and preventive medicine are the principles of ecology applied to the preservation of the public health.

The time is fast approaching when ethics, the science of right-living, will no longer seek its basis in metaphysical principles of right and wrong; for it will be recognized that true morality, as well as mental and bodily health, depend on conformity, conscious or unconscious, with the principles of Biology.

Robert Payne Bigelow.

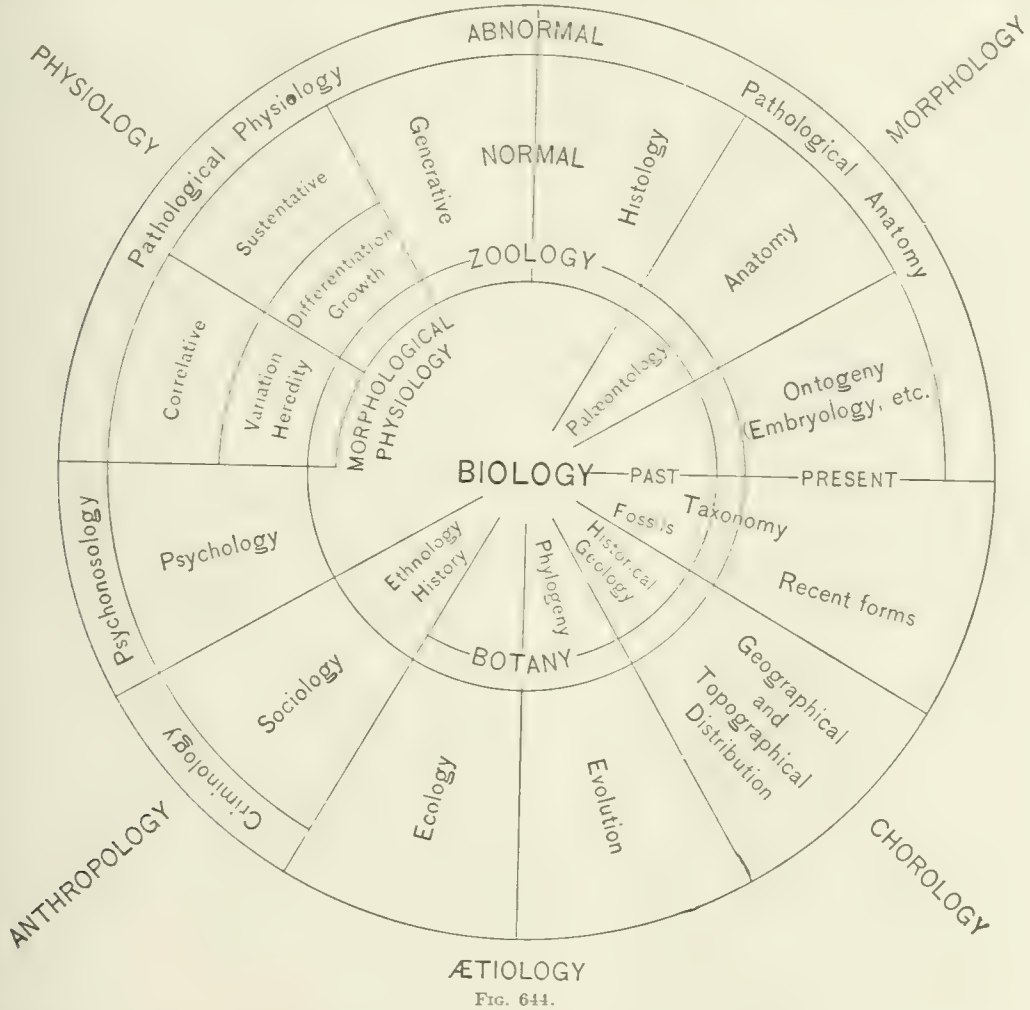

Fig. 644.

LITERATURE.

The literature of biology is already enormous and is growing larger every year. It may be well, however, to mention here a few useful works of reference.

For a brief history of biology see J. A. Thomson: "The Science of Life," 1899; Locy, "Biology and its Makers," 1908; Rádl, "Geschichte der biologischen Theorien," 1905–9.

Good elementary treatises on general biology are Huxley and Martin: "Practical Biology"; T. J. Parker: "Lessons in Elementary Biology"; and Sedgwick and Wilson: "General Biology," second edition.

More extended treatment of general problems will be found in E. B. Wilson: "The Cell in Development and Inheritance," second edition; M. Verworn: "General Physiology," translated by Lee; C. B. Davenport, "Experimental Morphology"; Y. Delage: "La structure du protoplasma et les théories sur l'hérédité et les grands problèmes de la biologie générale"; C. L. Morgan: "Animal Life and Intelligence."

For philosophical discussion see H. Spencer: "Principles of Biology," second edition, 1900; W. K. Brooks: "The Foundations of Zoology"; K. Pearson: "The Grammar of Science," second edition, pp. 328–532; H. Driesch, "Science and Philosophy of the Organism," 1908.

Additions to the science are recorded annually in L'Année Biologique, edited by Delage, Paris, since 1895; in "Ergebnisse der Anatomie und Entwickelungsgeschichte," edited by Merkel and Bonnet, Wiesbaden, since 1891; Ergebnisse der Physiologie," edited by Asher and Spiro, Wiesbaden, since 1902.

Biopsy.—This term was introduced into dermatology by Besnier to denote the diagnostic excision of a bit of skin of sufficient size to permit of a prompt histological study, but not large enough to require suture or occasion a cicatrix. The use of this term might readily be extended to include the diagnostic excision of tumors by the surgeon, but while in the latter case the method is used only as a last resort, in dermatology the excision of a bit of skin is practised by some almost as a matter of routine. Thus Darier, writing many years ago, announced that he personally had practised over 500 "biopsies."

The use of biopsy in dermatology must be somewhat restricted, because he who resorts to it ought to be a master of histology and histological technique. In theory it is a desideratum that a specimen be prepared, mounted, and examined during the period of the office visit; but this is hardly practicable, for the technique for such rapid examination does not lend itself to the work in hand. The minuteness of the fragment examined is not adapted to the freezing microtome; and the specimen therefore requires a little hardening in alcohol. After several hours, and *a fortiori* on the following day, or before the next office visit, a few free-hand sections may be made with the razor by compressing the fragment of tissue between two pieces of elder pith. A quick stain, like picrocarmin, is then employed and the specimen mounted in glycerin.

Darier recommends that a fold of skin be pinched up, after which a suitable knife transfixes it below the part to be examined. The latter is then cut loose with the knife aided perhaps with scissors. He has tried many hemostatics and gives preference to powdered juniper wood which has been saturated with creosote fumes. Suture is seldom required, the wound being covered with a little antiseptic gauze and sealed with collodion. Pain can be avoided by ethyl chloride anesthesia.

Material for biopsy of the deeper tissues is sometimes obtained by means of a barbed instrument (the "harpoon") which is plunged into the tumor to be examined and then withdrawn, bringing with it a bit of tissue. The examination of the muscles of hogs for trichinosis may also be mentioned here as a phase of biopsy.

As for the diagnostic possibilities of biopsy these are without limit; but naturally those of the greatest significance have reference to the indications or contraindications for surgical intervention. In this connection it is readily seen that modern biological reactions may make it possible to do away with much biopsy. Thus in a diagnosis between syphiloma and cancer a positive Wassermann reaction would perhaps render a biopsy unnecessary. Biopsy has been much used in differentiating between carcinoma, tuberculosis, and syphilis, and has not yet been, and perhaps may never be, quite supplanted by serodiagnostic tests. EDWARD PREBLE.

Birch.—The common name of the genus *Betula* (fam. *Betulaceæ*), of some thirty-five species, several of which are strongly aromatic. Unless otherwise specified, the *B. lenta* L., Sweet Birch or Cherry Birch (incorrectly "Black Birch") is to be understood. This is an abundant shrub or small tree in Eastern North America. Its bark is an important article of commerce, and has long been used medicinally as well as for flavoring. It contains a volatile oil identical with that of wintergreen, which see. The leaves of the European birch are considerably used as a diuretic.

The wood of several species is used as a source of medicinal tar, which, like that of beechwood, is rich in guaiacol. HENRY H. RUSBY.

Birch-Hirschfeld, Felix Victor.—Born in Cluvensieck, Germany, on May 5, 1842. In 1867 he received the degree of Doctor of Medicine from the University of Leipzig. Subsequently he held various positions of minor importance in the latter city and in Dresden, until finally, in 1885, he was called to the University of Leipzig to fill the Chair of General Pathology and Pathological Anatomy left vacant by the decease of Cohnheim. He held this chair up to the time of his death, which occurred on November 20, 1899.

Birch-Hirschfeld was one of the most distinguished pathological anatomists of the nineteenth century. He wrote valuable papers on cancer of the testicle, on emboli composed of tumor tissue, on the nature of cylindroma, on acutely developed tumors of the spleen, on pyemia, and on syphilis of the new-born. He also published a large text-book entitled "Lehrbuch der pathologischen Anatomie," 5th edition, Leipzig, 1896–1897. A. H. B.

Birth, Order of, with Reference to the Incidence of Disease.—The subject of the relationship between the numerical position of an individual among the children of a family and any diseases which that individual may contract, is a matter that has been given very little attention. Statistical information regarding this relationship is exceedingly meager. Mulhall's "Dictionary of Statistics" contains nothing that may enlighten one on this question. The same is true of the text-books on pathology, general medicine, and pediatrics. The reasons for this paucity of knowledge reside in the following facts: (1) There is a general impression that no clinical or diagnostic significance attaches to the order in which a person may be born—that there are so many other and more variable factors in the production of disease that the fortuitous order of birth can be of but trifling interest to the physician. (2) Clinical records which in many instances indicate the number of children in a given family, and less frequently state the diseases from which these may have suffered, almost invariably fail to mention the ages of the different children in the family. In view of the facts which a careful study of this question brings to light, a plea should be made for the more careful registration in clinical records of all possible information that may aid one in studying the vexed problem of the susceptibility to disease.

Without any definite experience to guide one in this practically unexplored field, one may nevertheless

reach a few definite conclusions based upon empirical observation and *a priori* reasoning. Thus, if the parents marry when very young and immature, and particularly if their means of livelihood are precarious, one would expect that their first offspring will be of feebler constitution than those that are born later. Similarly if a woman gives birth to a large number of children it is quite natural to suppose, and this supposition is corroborated by experience, that the children that are born late in the reproductive life of the woman, when her strength has been sapped by frequent gestation and parturition, and by the cares of a large household, are apt to be weaker and more subject to disease than the children that have come into the world earlier. Among the poorer classes, in large families in which the children are born at brief intervals, rachitis is apt to be manifested by the later children. The incidence of this disease is to be attributed partly to the maternal exhaustion attendant upon frequent child-bearing, which exhaustion is particularly apt to occur in the case of the calcium and phosphatic content of the maternal organism, and partly to the abject environment of the overcrowded household. In the case of syphilitic parents the first offspring are more apt to inherit the disease than those that are born later, owing to the fact that the parents usually undergo treatment after the mother has had one or more miscarriages, or after she has given birth to one or more syphilitic children. Another factor in the determination of the order in which disease may appear among children is the degree of intelligence of the mother, who profits by the experience with her first-born in the care of her subsequent children. This care is particularly of moment in the prevention of nutritional disturbances and gastroenteric disease. It should also be borne in mind that, other things being equal, the larger the family the greater are the chances of zymotic infection. Thus as the family grows in size the greater is the overcrowding and the greater become the chances of contact infection. Moreover, it is a common observation that the larger children who attend school are apt to bring home the common exanthemata and to impart these to the younger members of the family. This may probably serve to explain why among the tenement population of a large city measles, diphtheria, and scarlet fever are found so frequently among young infants. On the basis of this observation one is justified in drawing the conclusion that the larger the family the greater is the liability for the later members to contract the various infectious diseases. This conclusion can be substantiated only by statistical study.

It may be asked, "Of what value would be the accumulation of a mass of statistical figures and of the generalizations that may be drawn from them, with respect to this subject?" The answer is that the question is not a purely academic one. In spite of the fact that the agencies in the production of disease are so numerous and variable, it is important that all of these factors should be known and recognized. In weighing the relative importance of the soil *versus* the seed, it is necessary to know every fact that may in any way bear upon the subject of susceptibility. The truth of this statement may be realized more than ever before in these days when such topics as the limitation in the size of the family, eugenics, social service, maternity rewards, and maternity insurance are being so freely discussed. From the viewpoint of the laws of succession that prevail in royal families, the question of the relative vigor of the heir-apparent when compared with the rest of the family is not an insignificant one. Likewise in countries in which the laws of primogeniture are operative, it is a matter of no little moment to know that at least in certain respects there is no biological justification for the retention of these laws. Karl Pearson who has made careful mathematical studies of available data pertaining to various phases of this subject, has reached the conclusion "that in certain cases at least of constitutional defects which are inherited the earlier members of the family are more likely to suffer than the later." On the basis of this observation it may be suggested that the decadence noted in certain of the reigning houses of Europe is to be attributed to this pathological aspect of primogeniture. Another important application of studies based upon the order of birth is to be found in the domain of insurance medicine. A reliable and extensive set of figures showing the relationship between disease and the order of birth may serve to throw light on the question of expectation of life and may help in the task of gauging the insurability of an applicant. In this connection it may be suggested that the insurance companies have at their disposal a mass of figures pertaining to this subject which cannot fail to be of great value when properly collated and analyzed.

In recognizing on the one hand the disadvantages to the youngest members of families that are abnormally large, it must be admitted on the other hand that there are certain hygienic, educational, and ethical disadvantages attending the children in families that are abnormally small. These disadvantages and others are particularly manifest when an individual is an only child. J. K. Friedjung[1] has made an interesting study of this phase of the subject. His observations were based upon the study of 100 children each of whom was an only child or "Lieblingskind," as the Germans say. Of these children only thirteen were fully normal. The remainder manifested various nervous phenomena of either a neurasthenic or hysterical nature. The emotion of fear was particularly conspicuous in these neuropathic children. Among the conditions frequently observed were restlessness, pavor nocturnus, malnutrition, obstinate anorexia, chronic constipation, colitis, urticaria, and severe pruritus. Friedjung attributes these morbid manifestations to the excess of tender care which these children receive, which conclusion suggests the proper prophylaxis and treatment. There is sufficient basis for the popular belief that the "spoiled," pampered, or coddled child is apt to be less vigorous than other children. For this reason the eldest child in a family in which there is no other child for a number of years, and the child whose isolation is brought about by the death of brothers or sisters suffers the same disadvantages as the only child.

The question of the order of birth bears an important relation to that of longevity. According to A. H. Stewart[2] "the age of one's parents at the time of one's birth appears to be a factor in one's longevity. Children born of parents who are between twenty and forty years of age are believed to possess the greatest vitality. This appears to apply especially to the age of fathers. Children born of mothers who are between twenty and thirty-five appear to have the greatest chance of survival, while children born of mothers who are under twenty or past thirty-five or of fathers who are past forty possess less vitality, and consequently have less chance of survival. The second, third, fourth, and fifth children are believed to have a better chance of survival than first-born or those born after the fifth. But later statistics seem to indicate that one's numerical position in the family is not as important as the age of the parents, especially of one's mother at the time of one's birth. About twenty-five per cent. of those centenarians whose family histories have been traced were the first children of their parents. If the children of primiparæ are smaller and less vigorous than those of multiparæ, as has been claimed, it is probably due more to the difference in the age, size, and physical vigor of the mother than to the number of births. There are good physiological reasons for the belief

that large families tend to longevity, since the production of a large family indicates a special physical vigor of the parents. "It has been shown by Miss Beeton and Karl Pearson[3] that the older siblings, *i.e.* children born of the same parents, live on an average four to five years longer than younger siblings. They state that "a brother born ten years before another brother has probably seven years greater duration of life. A sister born ten years before another sister has probably six years greater duration of life."

The most intensive studies with reference to the relationship between the order of birth and any particular disease have been made in the case of tuberculosis. To W. C. Rivers[4] we are indebted for a scholarly review of this aspect of the subject. Rivers had noticed in examining the case histories of a large number of tuberculous patients at the Crossley Sanatorium that a considerable proportion of these were eldest-born children. He submitted his material to the expert biometrician, Karl Pearson,[5] who concluded from the figures that both first- and second-born offspring appear subject to consumption at a very much higher rate than younger members of a family. (See Table 1.) This conclusion is at variance with

Table III.

Order of birth.	Subjects.	Phthisical patients.	
		Expected.	Actual.
1	263	41.5	53
2	259	40.9	47
3	246	38.9	41
4	222	35.1	30
5	190	30.0	38
6	160	25.3	22
7	118	18.6	16
8	88	13.9	8
9	55	8.6	5
10	31	4.9	2
11	25	3.1	1
12	5	0.7	0
13	2	0.3	0
14	1	0.1	0
15	1	0.1	0
16	1	0.1	0

In commenting upon these results, Pearson observes that "if this special incidence on the earlier born be

Table I.

Siblings' order.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	Above 14
Number of cases observed	113	79.	41.	52.	39.	18.	18.	9.	3.	3.	3.	1.	1.	1.	0
Number of cases calculated.	67.1	64.4	58.5	50.9	43.5	32.6	22.2	15.1	10.0	6.2	3.7	2.6	1.6	1.1	1.6

what has been taught on the authority of the great German phthisiologist, Brehmer. The latter was of the impression that although in certain instances scrofula affected the earlier offspring, in large families the late-born were especially liable to contract tuberculosis. This susceptibility was, he thought, greatest in the sixth child. Brehmer's observations were made offhand and were not based upon exact statistical analysis. Pearson applied careful mathematical methods to 500 cases reported by Brehmer[6] and found that there is an excess of tuberculosis in the first-, second-, and sixth-born. A third series of cases was that afforded by Riffel's[7] records of several generations of the populations of south German villages, and analysis of these cases shows that first-born children present a larger proportion of tuberculosis than any of the rest. The value in this connection of the cases reported by Riffel is increased by the fact that this observer also recorded the relative ordinal incidence among the children of the same families with reference to pneumonia, typhoid fever, cancer, and trauma. His results are indicated in Table II as modified by Rivers. This table shows that of the five conditions investigated the only one besides tuberculosis that presents a greater incidence in the first-born is cancer. Rivers' own later material included 263 cases of tuberculosis. The results of the analysis of these are indicated in Table III.

Table II.

Deaths from	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
Phthisis	6.3	5.	5.2	5.1	5.2	5.7	5.	4.8	3.4	3.3	3.3	6.2
Pneumonia	1.8	2.5	2.0	1.5	1.3	2.1	2.1	1.8	0.8	2.6	0	0
Typhoid fever	1.2	0.7	1.2	0.7	0.5	1.3	0.4	0.6	1.7	1.3	1.1	0
Cancer	1.2	0.8	1.1	0.9	0.4	0.5	0.6	0.3	1.2	1.3	0	0
Trauma	0.1	0.7	0.6	0.4	0.6	0.5	0.6	0.7	0.4	0	0	2.

found to be true for other forms of pathological heritage, we have here a very serious factor of national deterioration introduced by the growing limitation of the family. It is further conceivable that any class which reproduces itself largely from elder children, *e.g.* the peerage, as far as the father is concerned, would tend on the average to degenerate more rapidly."

Rivers has carefully reviewed the available literature concerning what he calls the pathological aspects of primogeniture, and to him we are indebted for many of the following statements. The references to the literature are given in his article. Sir A. Mitchell found among 443 idiots and imbeciles that 31.1 per cent. were first-born. This observer concluded that idiocy is more likely to occur among first and latest pregnancies than among others. Matthews Duncan found that first-born children in Scotland are shorter and lighter than others but traces this to the influence of the early age of the mother. Heron made a study of Urquhart's 331 family trees of lunatic asylum patients in which he found excess of insanity among the four eldest children in a family. Carman after examining 1507 Michigan school children found that in general sensitiveness to pain decreases in order of birth. Wells studying data furnished by trained observers and by teachers of school children in California, gives curves showing with minor sex differences, first-born children superior to others in weight, height, association time, discrimination, voluntary motor ability, natural mental ability, neatness, and deportment. Macdonald stated that of fifty-three university students the first-born were more sensitive to pain than the second-born. Pearson notes that albinism occurs most frequently in eldest-born. Galton refers to the relative sterility of heiresses. Dugdale is quoted by Havelock Ellis as finding that criminality favors the first-born child. This observation is confirmed by Winter, who found that thirty out of

fifty-four criminals were first-born. Davidson found ten out of nineteen cases of congenital pyloric stenosis to be in eldest children.

In summing up his study Rivers concludes that "an innate tendency to consumption, a soil intrinsically suitable to the tubercle bacillus, and not the result of weakening by other disease, is an idea which has always had support. Bacteriological work may have limited the influence to be properly assigned to this predisposition; nevertheless, the theories of the *habitus phthisicus*, as stenosis of the upper thoracic aperture, the frequency of a small heart, of a condition of underweight, of supernumerary nipples and of nasal defects, have never been confuted. Eldest-born incidence might unite all these as coordinate degenerative manifestations; and eldest-born incidence apparently disposes of the objection, first advanced by Cohnheim, that the *habitus phthisicus* is the result of an already existing tuberculous infection." ALEXANDER SPINGARN.

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Birth Palsy.—See *Palsies, Infantile Cerebral.*

Births, Statistics of.—See *Vital Statistics.*

Biskra.—This is a place of growing importance situated on the outskirts of the Algerian Sahara, at an elevation of about 360 feet above sea level, in Lat. 35° 27′ N., and Long. 3° 22′ E. It consists of a union of several villages containing in all 8,000 inhabitants. It lies among plantations of date palms and evergreen trees, with gardens and squares containing tropical plants such as the yucca, the false pepper plant, the fragrant gum trees, and palms. Nearby are mountains capped with snow for the greater part of the year, and to the south the limitless expanse of the desert. Biskra is reached by steamer from Marseilles to Algiers in twenty-six hours, and by rail from the latter place in two days. One can break the journey at Constantine, which is about half-way. One can also reach Biskra by automobile. There are good hotel accommodations, and one can find endless diversion in the Oriental life and scenes of the various tribes which collect here—the shepherd Arab, the Nomad, the Moor, and the African. There are also to be found numerous remains of Roman occupation. The water supply is derived from wells, one of which, in the great mosque, is said never to be dry. According to Weber and Foster, the water contains too much salt for drinking and for certain cooking purposes.

The climate partakes of that of the desert, being warm, dry, equable, sunny, and rather bracing. "It is much drier and sunnier than the neighborhood of Algiers itself: but it is subject to violent winds which for days together may prevent outdoor exercise" (Weber and Foster). The season extends from October to April, and the temperature for these months, for the years 1887 to 1891, is given by Hurabielle ("Biskra," Paris, 1899) as follows:

	Maximum.	Minimum.	Mean.
October.....	81.2° F.	58.6° F.	70.0° F.
November..	69.0	48.0	57.9
December..	60.5	42.0	50.8
January...	58.6	39.7	48.8
February...	62.0	42.0	52.6
March.....	77.5	48.4	59.3
April.....	77.7	54.0	66.0

The following comparison is made with the temperature of Nice:

	Maximum.	Minimum.	Mean.	Rainfall.
Nice.....	67.7° F	36.8° F	52.0° F.	3.9 inches.
Biskra.....	60.5	47.6	58.4	0.6 inch.

The rainfall is almost *nil*, and the relative humidity must be very small. We have then at Biskra, during the winter season, or from October to April inclusive, a dry pure atmosphere, a mild and very equable temperature, practically no rain, and almost constant sunshine. "For six months," says Murray, "the climate is delicious. In the whole of Algeria one does not find a more agreeable temperature, a clearer sky, or more beautiful vegetation." The most considerable drawbacks are the high winds from the south and west, which are frequent. One is, however, partially protected from them in the interior of the oasis by the forest of date palms, which covers an area of 12,000 square meters.

The diseases which are relieved by a residence in this climate are certain cases of pulmonary tuberculosis, albuminuria, rheumatism, neurasthenia, climacteric disturbances, etc. There is no evidence that malaria exists at Biskra. "Biskra is suitable," says Huggard, "rather for valetudinarians than for invalids. For Europeans it can hardly compete in attraction with the Egyptian resorts such as Assouan, Luxor, Mena House, or Helonan."

The writer would acknowledge his indebtedness in the preparation of this sketch to J. Madison Taylor's article "Biskra," in the *Climatologist* for 1891; to "Au pays du bleu," Biskra, par L'Abbé Jean Hurabielle, Paris, 1899; and to the article upon "Climate in the Treatment of Disease" by Sir Hermann Weber and Dr. M. G. Foster, in Allbutt and Rolleston's System of Medicine, vol. i., 1905.

EDWARD O. OTIS.

Biskra Button.—See *Oriental Sore.*

Bismuth.—Bismuth is a metallic chemical element, with the symbol Bi, and atomic weight 208.5. It occurs free, also as the oxide and sulphide, Bi_2O_3 and Bi_2S_3. It is hard and brittle, and crystallizes in rhombohedra. It is frequently contaminated with arsenic.

GENERAL MEDICINAL PROPERTIES OF COMPOUNDS OF BISMUTH.—Experiments upon animals have shown that impregnation of the blood with bismuth produces poisonous effects generally similar to those wrought by other heavy metals. So far, however, as concerns the compounds of bismuth used in medicine, these, if pure, can be given with great freedom without constitutional disturbance—a fact commonly, and probably correctly, accounted for by the great insolubility of these compounds, by reason of which absorption of the mineral is both feeble and slow. Locally, soluble bismuth compounds are astringent and irritant, and the insoluble ones soothing, healing, and antiseptic. But if applied abundantly to exces-

sive wound surfaces, the insoluble compounds are capable of producing constitutional effects—acute stomatitis, catarrh of the intestines, and nephritis. Taken internally, bismuth compounds allay gastric pain or nausea, and tend to check diarrhea.

Compounds of Bismuth Used in Medicine.—The compounds of bismuth official in the United States Pharmacopœia are the *citrate, bismuth and ammonium citrate,* the *subcarbonate,* the *subgallate, subnitrate,* and *subsalicylate.*

Bismuth Citrate, $BiC_6H_5O_7$.—This salt is official under title *Bismuthi Citras,* chiefly for the purpose of making the next-to-be-named compound. Bismuth citrate is made by boiling the subnitrate in a solution of citric acid. It is "a white amorphous or microcrystalline powder, odorless and tasteless, and permanent in the air. Insoluble in water or alcohol, but soluble in ammonia water, and in solutions of alkali citrates" (U. S. P.). Dose, 0.125 gram (two grains). By dissolving this salt in water of ammonia, filtering, evaporating to a syrupy consistence, and spreading the syrupy fluid on glass plates to dry, a dry film breaking up into scales is obtained, analogous to the scale preparations of iron. These scales are official under the title:

Bismuthi et Ammonii Citras, Bismuth and Ammonium Citrate. They appear as "shining, pearly, or translucent scales, odorless, having a metallic taste, and becoming opaque with loss of ammonia on exposure to the air. Very soluble in water, and sparingly soluble in alcohol" (U. S. P.). The compound should be kept in small tightly stoppered bottles, and away from the light, for on exposure it loses ammonia, and then fails to dissolve wholly in water. The chemical composition, as in the case of the analogous preparations of iron, is obscure; some regard the scales as containing a true double citrate of the bases, and others consider them as a mere admixture.

This preparation is unique as being a soluble compound of bismuth. It is used internally for diarrhea, and, in medicinal dose, proves astringent and mildly irritant. The dose ranges from gr. i.–iii. (0.06–0.2).

Bismuth Subcarbonate, $(BiO)_2CO_3H_2O$.—This salt is official as *Bismuthi Subcarbonas.* It is "a white, or pale yellowish-white powder, of somewhat varying chemical composition, odorless and tasteless, and permanent in the air. Insoluble in water or alcohol, but completely soluble in nitric or hydrochloric acid, with copious effervescence. When heated to redness, the salt loses water and carbon dioxide, and should leave not less than 90 per cent. of a yellow residue which is soluble in nitric or hydrochloric acid, and blackened by hydrogen sulphide" (U. S. P.).

Bismuth subcarbonate is substantially a duplicate of the subnitrate in all its properties, and may be used for the same purposes and in the same manner as the latter salt.

Bismuth Subgallate.—This salt, approximately $Bi(OH)_2.C_7H_5O_5$, is official as *Bismuthi Subgallas.* It is widely known as *dermatol.* It should yield between fifty-two and fifty-seven per cent. of pure bismuth oxide. It is "an amorphous, bright yellow powder, somewhat variable in chemical composition, without odor or taste, and permanent in the air. Insoluble in water, alcohol, and ether; readily soluble with decomposition in hydrochloric, nitric, and sulphuric acids, if these be heated; insoluble in very dilute mineral acids; readily soluble in solutions of the alkali hydroxides, forming a clear yellow-colored solution, which rapidly changes to a deep red" (U. S. P.). Bismuth subgallate is used as an astringent sedative, also as an external application in eczema and for wounds and ulcerations. Dose, gr. iv. (0.25).

Bismuth Subnitrate, $BiONO_3,H_2O$.—This salt is official as *Bismuthi Subnitras.* It is "a white powder, of somewhat varying chemical composition, odorless and almost tasteless, and permanent in the air. Almost insoluble in water, and insoluble in alcohol; but readily soluble in nitric or hydrochloric acid. When heated to 120° C. (248° F.) for twelve hours, the salt loses not over three per cent. of moisture; when subsequently heated to redness, it evolves nitrous vapors, leaving not less than eighty per cent. of its weight of a yellow residue which is soluble in nitric or hydrochloric acid, and blackened by hydrogen sulphide. When brought in contact with moistened blue litmus paper, the salt shows a slightly acid reaction" (U. S. P.). This salt should not be prescribed with potassium iodide nor with the carbonates of the alkalies. Specimens of poor quality are apt to contain variable proportions of arsenic, even enough, it may be, to cause distinct poisoning in therapeutic doses. To detect this contamination, treat the specimen with sulphuric acid, evaporate to dryness, dissolve the residue in hot distilled water, and test the solution by Marsh's test for arsenic.

Bismuth subnitrate produces the effects of the insoluble bismuth compounds already described, and is the principal medicinal preparation of the metal. The only peculiarities of its action are the production of a garlicky odor to the breath of the taker, and a blackening of the stools. The salt is given internally in doses of wide range, from gr. v.–ʒi. (0.3–4.0), taken as a powder or suspended in mucilage. The pharmacopœial dose is gr. vii. (0.5). Externally it is used as a dusting powder in excoriations and sores, or, suspended in water, ten-per-cent. admixture, in the treatment of wounds.

Bismuth Subsalicylate.—This salt, approximately $Bi(OH)_2.C_7H_5O_2$, is official as *Bismuthi Subsalicylas,* and should yield not less than sixty-two and not more than sixty-four per cent. of pure bismuth oxide. It is "a white, or nearly white, amorphous or crystalline powder, odorless, tasteless, and permanent in the air. Almost insoluble in cold water; upon prolonged boiling with water a portion of the salicylic acid passes into solution with the formation of a more basic bismuth salicylate. It is partly soluble with decomposition in hydrochloric and nitric acids, a white, flocculent precipitate of salicylic acid separating. When heated at 120° C. (248° F.) bismuth subsalicylate should not lose more than one per cent. of water, and on subsequently heating to redness it at first chars, finally leaving a yellow residue, which is soluble in hydrochloric or nitric acid and is blackened by ammonium sulphide (U. S. P.). It is used as an intestinal antiseptic, in doses of from five to fifteen grains. The pharmacopœial dose is gr. iv. (0.25).

Toxicology.—The two most important compounds of bismuth are the subnitrate and the subcarbonate. These preparations are extensively used, in doses of gr. x. to lx. (0.6 to 4.0), or more, in the treatment of diarrhea and other forms of intestinal irritation. The subnitrate of bismuth was considered an active poison by many of the earlier writers, who state that symptoms of gastroenteritis frequently follow its administration in doses of ʒss. to ij. (2.0 to 8.0) daily. A case is recorded in which two drams of this substance, administered to an adult, caused severe symptoms of irritant poisoning, followed by death on the ninth day. At the postmortem examination the tonsils, uvula, pharynx, and epiglottis were found gangrenous; the esophagus and stomach were very red, and the whole intestinal canal was red, and here and there gangrenous, especially at the rectum (Christison).

As the subnitrate and subcarbonate of bismuth are used very freely without any bad results, it is doubtful if they can be considered irritants even in comparatively large doses. The best authorities of the present day generally agree in attributing the effects noticed by the earlier writers to impurities in the drug, chiefly arsenic, but also lead and antimony.

Taylor found arsenic in three samples of subnitrate of bismuth out of five examined by him; Rogers, in eight samples out of ten. Herepath examined fourteen samples and found arsenic in all. Salisbury found arsenic in thirteen samples out of eighteen; he also examined five samples of the subcarbonate of bismuth and found arsenic in all.

There can be no doubt that the symptoms produced by subnitrate of bismuth have been sometimes due to the arsenic which it contains. Salts of bismuth containing 0.129 per cent. arsenic, however, have failed to produce symptoms of poisoning when administered to dogs in doses of fifteen to thirty grams (Parral and Garnier). It is possible, therefore, that the bad effects which have been caused by these preparations are to be attributed, in some cases at least, to other causes. Idiosyncrasy has been suggested. Monneret thinks they may be due, in certain cases, to an exacerbation of the trouble for which the bismuth was administered. It has been suggested that an excess of free acid in the stomach, or acid salts, administered simultaneously with the subnitrate, may, in some cases, have converted the latter into a soluble poisonous salt of bismuth. Sobernheim explains the poisonous effects in a fatal case related by Christison, by supposing that the bitartrate of potassium, which was administered with the subnitrate of bismuth, converted the latter into an acid nitrate, which is shown by experiments on animals to be an irritant poison. Herbelin has found considerable free nitric acid in subnitrate of bismuth. The presence of this acid, or of the normal or acid nitrate, in specimens which have been carelessly prepared, may also explain some of the symptoms which have been observed.

Preparations of bismuth are frequently administered in the treatment of gastroenteritis caused by the metallic irritants. The discovery of arsenic in the subnitrate of bismuth thus administered has been sufficient to invalidate the results of the chemical analysis in certain cases of alleged poisoning by arsenic, in which the amount of arsenic detected in the organs was small (Rogers, Reese). The attempt to account for the presence of arsenic in the body by suggesting that it may have come from the bismuth administered, is frequently made. It is important, therefore, whenever these preparations have been given in cases of suspected poisoning, to preserve a sample for subsequent analysis, if necessary.

The subcarbonate of bismuth, if pure, is undoubtedly as free from irritant properties as is the subnitrate. It is, however, more soluble than the subnitrate, and is, therefore, more liable to become converted into a soluble salt of bismuth by the acids of the gastric juice, or by acid salts if these are administered simultaneously with it. As the soluble salts of bismuth are poisonous, the subnitrate would appear to be the safer preparation when large doses are to be administered, or when the administration is to be continued for a long time.

Under the name "pearl white" the subnitrate of bismuth is used to a considerable extent as a cosmetic. The subcarbonate and oxychloride of bismuth are sometimes used for the same purpose. There is no evidence to show that they are absorbed through the skin, or that they produce, if pure, any injurious consequences, aside from stopping up the pores and thus interfering with the healthy action of the skin. Bismuth preparations containing arsenic or lead might, however, produce injurious effects when used as cosmetics.

Experiments on animals show that the soluble salts of bismuth are poisonous. The action of the following salts has been investigated: the nitrate (Orfila), the citrate of bismuth and ammonia (Stefanowitch, Lebedoff, Feder-Meyer, Mory), the acetate (Bricka), and the tartrate of bismuth and potassium (Rabuteau). The symptoms which follow the administration of these salts do not differ materially from those produced by the metallic irritants generally. The most constant postmortem appearances are inflammation of the stomach and intestines, and a more or less extensive fatty degeneration of the liver, kidneys, and heart. Lebedoff states that the glycogen disappears from the liver after the long-continued administration of the citrate of bismuth and ammonia. The red blood corpuscles in animals poisoned by this compound present a finely granular appearance, and masses of small free granules may be seen in the serum. These appearances point to the destruction of the blood corpuscles (Feder-Meyer).

Absorption and Elimination.—When subnitrate of bismuth is administered, the greater part is separated with the feces, either unchanged or in the form of sulphide. A part is absorbed. Orfila detected bismuth in the liver, spleen, and urine of dogs to which the subnitrate had been administered. Bergeret and Mayençon state that, when the subnitrate is administered, bismuth can always be detected in the urine after a few hours. They also detected it in the serous exudation of dropsy. When a few grains are given to rabbits, it can be found, in from twenty to thirty minutes, in the urine, spleen, blood, and muscles, and even eight days after the administration it can be detected in all the tissues. The last-named authorities detected traces in the liver and kidneys of a man who had taken one gram of the subnitrate five days before death, but they failed to find it in the body of a woman who died sixty-two days after the ingestion of two grams (quoted by H. C. Wood, Jr.).

After the administration of the soluble salts of bismuth, the metal has been detected in the urine, feces, saliva, stomach, liver, spleen, and bones. It can be detected in the liver many months after the last administration (Bricka). It is eliminated with the urine, feces, and, according to Dubinski, with the saliva.

EDWARD CURTIS.
R. J. E. SCOTT.

Bistort.—The rhizome of *Polygonum bistorta* L. (fam. *Polygonaceæ*).

The rhizome is covered with roots. It is as large as the little finger, from five to fifteen centimeters long (two to six inches), somewhat flattened, transversely wrinkled, variously, often excessively, once or twice doubled upon itself like the letter S. When dry it is hard and brittle, dark brown externally, reddish or purplish within, with a single circle of well-marked woody bundles; taste, astringent; odor, slight.

It contains about twenty per cent. of tannic and a little gallic acid, and was formerly used as a source of starch. It has been a well-known and considerably used astringent but is now little used.

Dose: gr. xv.–xxx. (1.0–20). H. H. RUSBY.

Bittersweet.—See *Dulcamara*.

Bittersweet, false or climbing, should not be confounded with Dulcamara, though its composition is in part similar. It is the bark of *Celastrus scandens* L. (fam. *Celastraceæ*), a very woody twiner, common in many parts of the United States. This is the "bittersweet" whose orange-colored fruits, after bursting open in the fall to display the handsome scarlet-arilled seeds, is largely used for decorative purposes. Its composition and properties are even less known than those of Dulcamara. Its active constituent is apparently a saponin-like glucoside, and it has been used in syphilis and hepatic disorders.

H. H. RUSBY.

Bizzozero, Giulio.—Born in Varece, Northern Italy, March 20, 1846. He studied medicine in Zürich and also in Berlin, and finally received the degree of

M. D. from the University of Pavia, Italy, in 1866. From 1868 to 1872 he acted as a temporary professor in the same university. In December of the latter year he was called to fill the chair of General Pathology in the University of Turin. He died April 8, 1901.

Bizzozero was a frequent contributor to medical literature, both Italian and German. Many articles from his pen will be found in the Wiener med. Jahrbücher, in the Centralblatt für die med. Wissenschaften, in Moleschott's Untersuchungen, in Virchow's Archiv, and in the Archiv für mikroskopische Anatomie. He founded the Archivio delle Scienze Mediche. The Pathological Institute of Turin, of which Bizzozero was the Director, was one of the most frequented in Italy. Among his pupils were such men as Golgi of Pavia, Tizzoni of Bologna, Griffini and Canalis of Genoa, Foà of Turin, Salvioli of Padua, and Morpurgo of Siena. A. H. B.

Blackberry.—See *Rubus*.

Black Flies.—Flies of the genus *Simulium*, also called buffalo gnats. The larvæ live in swift flowing streams. The adult flies are fierce blood suckers; their bite is not only painful, but it also usually causes profuse bleeding. A poison is injected into the wound which causes severe swelling and has been known to produce systemic infection. By those holding the protozoan theory of pellagra, the pathoganic cause of the disease is believed to be transmitted by a species of Simulium. See *Insects, poisonous*.

A. S. P.

Blackwater Fever.—*Synonyms*: Hemoglobinuric malarial fever, Malarial hemoglobinuria.

Definition.—A disease or form of disease associated with malarial infection, caused possibly by an invasion of some special form or forms of malarial parasites, and characterized by fever, jaundice, and hemoglobinuria.

Geographical Distribution.—The disease was first described early in the nineteenth century by French naval surgeons stationed at Nossibé, an island off the northwest coast of Madagascar. It is prevalent in the flat coast regions of tropical Africa, especially on the Gold Coast and in the Congo basin, and is said to be increasing in these regions of late years. It is encountered in Southern China, in some districts of India, in Siam and the East Indies, and in Asia Minor. Cases are occasionally seen in Greece, Italy, and Spain. The disease is not unknown in the Southern United States. It is not uncommon in the West Indies; and on the Isthmus of Panama it causes a considerable number of deaths every year. Hemoglobinuric fever is found only in regions where malaria is exceedingly prevalent in its severer forms. And it is not found in all of such regions. For instance, malarial fever prevails throughout India; but only in certain notorious districts in Assam, Upper Burmah, and the Terai is blackwater fever encountered. In other regions of India it is practically unknown. The same is true of British Guiana. Laveran never saw blackwater fever in Algeria.

Etiology.—It is quite generally accepted now that blackwater fever is a form of malaria. It occurs only in malarial regions; and if examination of the blood has been made in time, competent observers have been able to demonstrate malarial parasites in nearly every case, though their specific characters were not always determined. Thus, in blood examinations made on the day preceding the hemoglobinuric attack, Stephens and Christophers[1] and Mannaberg[2] have found parasites, either estivo-autumnal, tertian, quartan, or of undetermined character, in ninety-five per cent. of cases. F. Plehn found parasites in sixteen out of nineteen cases examined on the first day of the disease, in two out of nine cases examined on the second day, and in none of six cases examined after the second day. Very early in the attack the disintegration of the infected corpuscles deprives the parasites of their corpuscular hosts and they perish in the plasma. Free hemoglobin is not present in the urine in health. In an infection with the subtertian parasites involving a very high percentage of the red corpuscles (twelve to fifteen per cent.), Brem has shown that free hemoglobin in the urine can be demonstrated chemically though the amount may be by no means sufficient to constitute clinically a case of blackwater. No other parasite than a malarial one has ever been found in the blood or organs. No case of blackwater fever has ever come to autopsy in which microscopic examination of sections of liver and spleen failed to show a deposit of malarial pigment.

All races are susceptible to the disease. Europeans are most susceptible, negroes least so: The European sojourner is seldom attacked during his first six months, and Crosse states that a first attack is rarely experienced after three years of residence. Children are seldom attacked, and women less frequently than men. After a prolonged residence in a tropical place where malaria and blackwater fever are prevalent and where the patient has suffered attacks of malaria in its ordinary forms, removal or return to a cold climate often results in an attack of blackwater fever. Bodily exertion, injuries, excesses, and all weakening influences predispose to attack as is the case with other diseases. Individual susceptibility probably varies. One attack predisposes to recurring attacks which almost invariably follow and one of which is likely to be fatal. Fisch has seen permanent recovery after ten or more attacks and believes that after the fourth attack there is a diminishing danger of fatal result.

The administration of quinine, even in small dosage, has sometimes acted as the immediate precipitating cause of the hemoglobinuria.

Pathology.—The very extensive and rapid destruction of red corpuscles in the attack is the dominant feature of blackwater fever. It has been suggested that the disease may be caused by a peculiar variety of the subtertian organism, morphologically undistinguishable from others as yet, and producing a peculiarly virulent hemolytic toxin. The hemoglobin released from the destroyed corpuscles in great quantities, being partly converted into biliary pigment in the liver, produces a jaundice and is largely excreted in an increased production of bile. Some is excreted through the intestinal walls (tarry stools). The hemoglobin, with the liberated toxin and soluble waste products, free in the blood-plasma, is excreted in great quantities by the kidneys, producing the typical "blackwater," a urine as dark as porter or stout, which produces a persistent pink or yellow froth on shaking the bottle.

Examination of the blood reveals poikilocytosis, with macrocytes and microcytes. Sambon has observed an absolute leucocytosis in some cases. The plasma is stained with hemoglobin in solution. The appearance of nucleated red cells is a sign of commencing regeneration. The hemoglobin falls rapidly, a hemoglobinuric attack frequently causing a loss of one-third of the existing percentage, even though that were already low. In a case of Brem's[3] the hemoglobin fell from forty-two to twenty-eight per cent. in twenty-four hours, and continued to fall till it reached seventeen per cent. The loss of hemoglobin is apt to continue for a day or two after the cessation of hemoglobinuria. Owing to the fact that corpuscular destruction takes place faster than the hemoglobin is eliminated by the kidneys or converted into bile pigment by the liver, the color index

is apt to be above normal during the attack, though it falls below normal later when blood regeneration has begun.

Postmortem, the kidneys of a rapidly fatal case are found to be enlarged and congested, "the tubules blocked with hemoglobin infarcts, the cells laden with yellow pigment grains."

Symptoms.—The *prodromes* are identical with those of a malarial attack, viz., malaise, lumbar pain, sense of heaviness and apathy, with mild headache and anorexia.

The actual commencement of the disease is usually with severe and prolonged rigor and rapid rise of temperature to 104° or 105°. In some cases the initial rise is slight, not exceeding 100°. The attack may even run a non-febrile course. There is restlessness, with sense of oppression and hopelessness. After a few hours there is usually a transient perspiration with only slight remission in the fever, followed by a second and perhaps even by a third rigor and exacerbation within the first twenty-four hours. Quite usually there will be one or two rigors on the second day, and often one on the third.

Generally from the beginning there is violent bilious vomiting with abdominal pain and intense thirst. There may be diarrhea, the stools being bilious and at times tarry from the extravasation of blood serum containing free hemoglobin into the intestine. Sometimes there is constipation instead of diarrhea. The liver is apt to be enlarged and tender to pressure especially over the gall bladder. Enlargement of the spleen is the rule, though it may be masked by intestinal distention, tympanites being a frequent condition in blackwater fever. *Jaundice* appears early, generally within the first twenty-four hours, and increases rapidly. It is seldom very deep in color and it usually disappears within a few days.

The urine is almost invariably markedly reduced in quantity. Very early in the attack, sometimes even before the outbreak of the fever, the *hemoglobinuria* appears, the urine being thick, opaque, and a yellow, red, or blackish-brown hue. It is usually, though not always, acid. The specific gravity is generally high, 1.030 to 1.032. The albumin, estimated by Esbach's method, is generally from 0.05 to 0.2 per cent. Biliary pigment and bile acid are often present. If the urine be shaken it forms a red or yellow froth. When allowed to stand, a copious sediment forms, which contains epithelium, grains and flakes of hemoglobin, hematoidin crystals, and hemoglobinuric casts. It is exceptional to find a few red blood-corpuscles. The evacuation of urine is frequent and painful. Occasionally there is complete anuria.

The attack inevitably produces a sudden and severe anemia, and the bodily strength is lost with corresponding rapidity. There is a small and irregular pulse with dyspnea, and hemorrhage from the nose is common; from the gums or in the skin hemorrhages are less common.

In fatal attacks, death is apt to occur during the second week of the disease. It may be the direct result of cardiac insufficiency, of thrombosis or embolism, or of the severe blood dyscrasia. From the inability of the kidneys to perform their function death sometimes ensues from *uremia* with all the usual symptoms of that condition.

The albuminuria persists usually for weeks, but in favorable cases the hemoglobinuria is transitory and the jaundice disappears rapidly. Recovery is slow, with a gradual regeneration of the normal blood elements. As the parasites have undergone destruction along with the corpuscles containing them, a convalescent case frequently remains free from malaria for a long time without the administration of quinine. Hemoglobinuric attacks have been known in several instances to terminate permanently a chronic malarial infection.

Diagnosis.—The presence of malarial parasites in the blood early in the disease, and their absence later, is an important fact. The presence of parasites in the peripheral blood after the second day of the disease, if the case be not seen earlier in the attack, is against a diagnosis of blackwater fever and in favor of ordinary bilious remittent malaria. The most important differential diagnosis to be made is that from *yellow fever*. The discovery of parasites by an early blood examination, and the enlarged and tender liver and spleen are against yellow fever. The sthenic features present at the outset of yellow fever, the throbbing headache, flushed face, injected conjunctivæ, congested gums tending to bleed at a touch, are absent in blackwater fever. The points for differential diagnosis may be tabulated thus:

Blackwater Fever.	Yellow Fever.
Asthenic.	Sthenic.
Spleen almost always enlarged and palpable.	Spleen not enlarged.
Liver enlarged and painful.	Liver enlarged, not painful.
Early vomiting bilious, not bloody.	Early vomiting acid and mucous.
No late vomiting.	Late vomiting bloody (*black vomit*).
Jaundice early, and always present.	Jaundice late, perhaps absent.
Hemoglobinuria, not hematuria.	Sometimes hematuria, but not hemoglobinuria.
Sporadic.	Epidemic.
Wide distribution.	Limited distribution.
Attacks old residents mostly.	Attacks new residents mostly.
Predisposes to further attacks.	Produces immunity.

Prognosis.—This is always grave. A mortality as low as four per cent. has been observed by O'Neill in Madagascar, but the usual mortality to be expected is much higher, usually from twenty-five to forty or fifty per cent. If a single attack followed by recovery is to be considered as a case treated (a large percentage of recoveries are returned on this basis) it should be remembered that if the patients were followed through subsequent attacks the individual mortality would be found to be much higher. According to Fisch, blackwater fever has become more frequent on the Gold Coast of late years, but the mortality has fallen from fifty to about twenty per cent. Favorable signs are the occurrence of only one or two brief febrile paroxysms lasting a few hours, and the rapid disappearance of the jaundice and hemoglobinuria.

Prophylaxis.—The prophylaxis of blackwater fever is the prophylaxis of malaria and has to do entirely with protection of persons from the bites of mosquitos. Individual prophylaxis is a question of screening, and public prophylaxis a question of mosquito extermination. We are not as yet in possession of any evidence that blackwater fever is due to any special form of parasite. The writer's view of the so-called *prophylactic* use of quinine is as follows: A very small daily dosage of quinine is often sufficient to inhibit the symptoms of the malarial paroxysm. In the malignant forms of malaria which prevail in the tropics this small dosage is not sufficient to cure existing infection. Such use of quinine does not, of course, bring about any sort of physiological immunity to disease. As a matter of military or other expediency, the efficiency of a force may often be preserved or enhanced by that small dosage of quinine which will inhibit symptoms without producing inconvenient cinchonism. But there is no acceptable evidence on record that this so-called prophylactic dosage will destroy the sporozoites implanted by the mosquito or prevent their further development. If malarial infection has taken place the patient needs more than this dosage for his cure. If no infection exists he needs no quinine at all.

TREATMENT.—The causes of death to be feared early in the attack are *kidney block*, and *heart failure*. The patient attacked should be put to bed at once and not moved after the first day. The surface of the body should be kept warm. Heat may be applied to the loins. Liquid must be given copiously in the form of warm drink or carbonated water if retained; otherwise saline injections preferably by rectum, if necessary by hypodermoclysis. The effort should be to get ℥vi. or ℥viii. of water per hour into the system, allowing for diaphoresis and hoping that half this amount will be excreted by the kidneys. Do not give diuretic drugs. The hemoglobin itself is a powerful diuretic. Do not give a cathartic till after the fourth day, when a saline may assist in the elimination of toxins and waste-products. The irregular secondary fever which follows the acute hemoglobinuric stage is not malarial but caused by waste-products. In high degrees of anemia oxygen inhalations, if available, may relieve alarming symptoms. Transfusion of blood has been successfully practised. Cardiac stimulants should not be given at the beginning, but later on, if needed, alcohol in a palatable form, strychnine, or digitalin may be used; and calcium chloride gr. xv. to xxx. every four hours may be given to restore tonicity of blood and of heart and kidney cells.

As regards the use of quinine it should not be forgotten that the disease itself destroys primarily those red corpuscles whose resistance is lowered by contained parasites, and destroys the parasites along with them. There is thus a tendency to spontaneous cure. On this principle, and remembering that quinine acts in some cases as a precipitating or secondary cause of hemoglobinuria, it is now quite generally accepted by those familiar with the disease that no quinine should ever be given during the hemoglobinuric attack, whether parasites are found in the blood or not. Lower mortality and better results are secured by adherence to this rule.

Two weeks after the attack, if any parasites can be found in the blood, give quinine very cautiously, one-quarter to one-half grain three times a day increased carefully to one grain until tolerance is established. Similar caution should be observed in treating any case of malaria with a history of blackwater. The best form of quinine for use is the bihydrochloride in solution of the strength of one to three and with an excess of acid, given intramuscularly. When a patient has recovered from an attack of blackwater fever it is advisable to remove him to a non-malarious place in a temperate climate. J. F. LEYS.

1. Practical Study of Malaria. London, 1904.
2. Malarial Diseases. Philadelphia, 1905.
3. Journal of the American Medical Association, 1906, xlvii., 1896.

Blackwell, Elizabeth.—Born in Bristol, England, February 3, 1821. When she was eleven years old her father brought his family to America to live, but died six years later leaving nine children in straightened circumstances. The three eldest girls, of whom Elizabeth was one, then supported the family, at the same time educating the younger children, by teaching school. When the boys had become self-supporting the school was abandoned, but Elizabeth continued to teach music for some years in order to earn enough for her medical education. She was taught anatomy by two medical students in Philadelphia and then sought admission to a medical school. Twelve schools, one after another in monotonous succession, refused her prayer for an education, but finally the Geneva, N. Y., Medical College received her, after having submitted her application to a plebiscite of the students. After once gaining the right to study here—somewhat to the chagrin, it is said, of the faculty who had not anticipated the favorable action of the students—she was treated with the utmost courtesy by professors and students alike. She received the degree of M. D. in 1849, being the first woman medical graduate in modern times. After graduation she spent two years in study in Europe, chiefly in France, the hospitals of her native country being closed to her as had been the schools of America. While at the Maternity Hospital in Paris she contracted a purulent ophthalmia from one of the patients, as a result of which she lost the sight of one eye.

On returning to this country Elizabeth Blackwell entered upon the practice of her profession, forming a partnership with her sister Emily after the latter's graduation in 1854. With Emily she established the New York Infirmary for Women and Children, out of which grew the first medical school for women in the world. In 1859 she revisited England and was now received cordially by many of the leaders of the profession, her name being admitted to the Medical Register as a recognized practitioner, she being thus the first woman physician to be registered in Great Britain. While there she delivered a number of lectures in the larger towns of Great Britain on Medicine as a Profession for Women At the outbreak of the American Civil War she took an active part with her sister in perfecting an organization for the nursing of wounded and invalided soldiers. In 1869 she returned to England to live, practising in London and Hastings. She then joined the staff of the New Hospital for Women and held the chair of Gynecology in the newly established London School of Medicine for Women. She died May 31, 1910.

FIG. 645.—Elizabeth Blackwell.

Dr. Blackwell wrote a number of articles and monographs on subjects relating to popular medicine, the moral and sanitary education of children, and medical education for women. Among the more formal treatises published by her were: "The Lesson of Life," 1852; "The Religion of Health," 1869; "The Physical Education of Girls"; "Moral Education of the Young," 1876; "Human Element in Sex," 1884; "Scientific Method in Biology"; and "Pioneer Work in Opening the Medical Profession to Women," 1895, the latter containing many interesting autobiographical details.

The New York Infirmary for Women and Children, founded by Dr. Blackwell, was organized January 30, 1854, its objects being: "1. To provide medical aid for the sick poor, especially women and children. 2. To secure the services of well-qualified female physicians in the care of sick women. 3. To form a school for training nurses." During the first three years only the dispensary for out-door patients was in operation, but in the spring of 1857 the Legislature of the State of New York voted an appropriation of $1,000 to the Infirmary, in common with appropriations to other city infirmaries, and a further amount being subscribed by friends of the institution, it was decided to open a hospital. A building was rented and the hospital was opened May 12, 1857. The attending physicians were Drs. Elizabeth Blackwell, Marie F. Zackrzewska, and Emily Blackwell. In 1865 the charter for a woman's medical college was obtained, and the first regular instruction was begun early in November, 1868, with a class of fifteen students. In 1898, the Cornell University Medical College having

opened its classes to women on equal terms with men, the college work in connection with the Infirmary was discontinued. Dr. Blackwell was not long actively connected with the college, although she held the chair of Hygiene in the faculty, as she went to England to live in 1869, but her sister, Dr. Emily Blackwell, was dean of the school for many years. During the thirty years of its existence the school numbered among its graduates many of the leading women physicians of this and other countries. T. L. S

Blackwell, Emily.—Born in Bristol, England, in 1826, but removed with her family to this country in 1832. Her struggles to obtain a medical education were indicative of the prejudices of the time. In 1851 she was refused admission to the Geneva Medical School, from which her sister had been graduated two years before, although the authorities were compelled to admit that the presence of Elizabeth Blackwell "had exercised a beneficial influence upon her fellow students in all respects." In succession ten medical colleges refused to enter her as a student, but finally she was permitted to attend some of the classes, though not as a regular student, at the Bellevue Medical College in New York, and a year later the Rush Medical College of Chicago consented to admit her as a candidate for a degree. This permission was later withdrawn, however, because of the censure of the Illinois State Medical Association. At length the Cleveland Medical College, the Medical Department of Western Reserve College, admitted her, and in 1854 she received the degree of doctor of medicine from this institution. After further study abroad Dr. Blackwell returned to practise in New York, and together with her sister undertook to provide facilities for other women to enter their profession. It was decided that the greatest need was for a hospital in which women might obtain the experience not offered to them elsewhere, but the proposal to open such an institution, in which the attending physicians should be women, was met by a storm of disapproval. All difficulties were, however, finally overcome, and in 1865 the New York Legislature granted a charter to the New York Infirmary for Women and Children, a number of eminent men physicians acting as a consulting board. In 1868 the Woman's Medical College was opened in connection with the Infirmary, and the first class was graduated in 1870. Dr. Blackwell was for many years dean of the college. In 1898 the college courses were discontinued. (See the sketch of *Elizabeth Blackwell*.) Dr. Blackwell remained on the consulting staff of the Infirmary until her death, which occurred at her summer home, York Cliffs, Maine, on September 8, 1910. T. L. S.

FIG. 646.—Emily Blackwell.

Bladder, Anatomy of the.—The urinary bladder presents a body, a neck, an apex, and a base, or bas-fond. It is sometimes absent as a distinct organ, owing to an arrest in the development of the parts, when it forms but one cavity with the rectum. It is never double. It may, however, extend in a constricted form up to the umbilicus in those cases of arrest of development in which the urachus fails to undergo obliteration.

In a general way it may be said that when distended to its full capacity, the bladder is about twice as large as the fist of the subject. In this description the organ will be supposed to be distended to its usual capacity.

It occupies the front part of the pelvic cavity and the lower part of the hypogastrium.

The direction of its axis, that is, of the line extending from the apex to the center of the base, is about the same as that of the upper strait of the pelvis, and therefore the same as that of the body and neck of the female uterus. The direction of the neck is forward, parallel to the line of the axis of the lower strait of the pelvis. The line from the apex to the orifice of the neck would be represented by a curved line corresponding to the curved axis of the cavity of the pelvis.

The bladder is held in its position by the connection of its neck with the pelvis through the short glistening fibers of fibrous tissue called the ligament of the bladder; also by the connection of the apex with the urachus and the umbilicus opening. The reflection of the peritoneum from the abdominal wall to the rectum, along its posterior surface and over the upper part of the lateral surfaces, assists in keeping the organ in position. The bladder is also supported by the rectum upon which the base rests. Thus fixed, it may expand and contract more or less, but it possesses no movement in its entirety.

The shape of the organ is more or less conical, with the base situated below. The anterior surface is in relation below with the posterior surface of the pubis, and, above the pelvis, with the abdominal walls, *i.e.* with the posterior surface of the rectus abdominis muscles. It is almost always free, in this locality, from peritoneal covering. There is a thin layer of fat between the walls of the bladder. The posterior surface is in relation with the peritoneum, with coils of the ileum, and with the rectum. The peritoneum forms there the rectovesical cul-de-sac.

The lateral folds of this rectovesical cul-de-sac are called by some the posterior ligaments of the bladder. They enclose the obliterated umbilical arteries and the ureters. The lateral surfaces are covered by peritoneum in the upper and posterior half and are there in relation with the coils of the ileum. But the lower and anterior half of these surfaces is free from peritoneum and is in relation with the pelvic areolar tissue. The obliterated umbilical arteries cross, obliquely downward, the lateral surface; the peritoneum does not extend in front of this cord. The spermatic duct curves backward along the posterior portion of the lateral surface, passing on the inner side of the ureter.

The apex gives attachment to the urachus. It is covered with peritoneum.

The base is in relation, on the middle line and in front, with the prostate and behind with the rectum. On the side it is in relation with the spermatic duct, seminal vesicles, and the ureters.

The bladder is of a white flesh color. It is a resistant organ; it is contractile. It presents first a peritoneal coat which invests only its apex, its posterior surface, and the upper part of the lateral surfaces. The anterior surface, the lower part of the lateral surfaces, the base, and the neck are entirely free from peritoneum.

The second coat is a muscular coat composed of three layers or sets of fibers. The superficial fibers are longitudinal in direction and are composed of three groups. The upper group comes from the urachus and spreads over the apex of the bladder. The anterior group comes from the pubis, to which they are attached by glistening aponeurotic fibers called the ligaments of the bladder; they spread over the anterior surface. The posterior group comes from the base of the prostate and expands over the posterior surface of the organ. The middle muscular

fibers are more or less circular. They are in greater number around the neck, where they form the sphincter of the bladder or vesical sphincter. They form a sort of elliptical sphincter around the orifices of each ureter. The last and innermost layer of fibers are the plexiform fibers, which have no definite direction. These fibers are not uniformly distributed over the organ, but form bundles more or less prominent which cross one another in all directions. Some of the bundles make quite a projection on the inner surface of the bladder, and may give rise to small pouches or alveoles. The muscular fibers are all of the smooth variety.

The submucous areolar layer is marked, but presents nothing special.

The mucous layer presents nothing of interest except at the base. There the organ presents posteriorly a slight depression called the bas-fond. In front is seen a triangular surface called the trigone; it corresponds to the prostate. The front angle corresponds to the urethra, and the two posterior angles to the openings of the ureters, remarkable

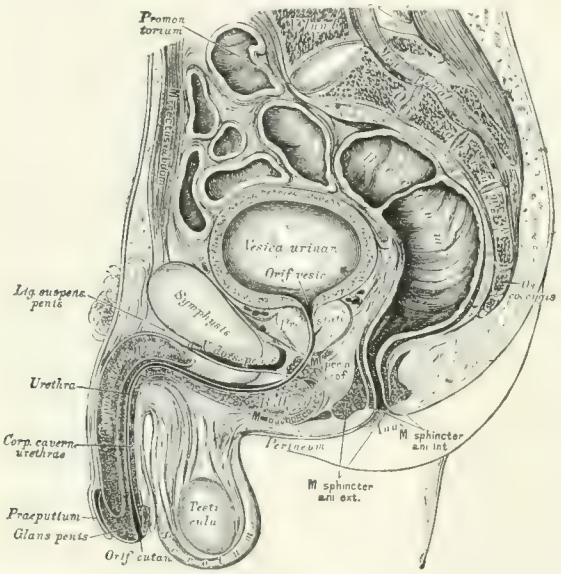

FIG. 647.—Sagittal Median Section through the Male Pelvis. About one-third natural size. (Heitzmann).

for their slit-like shape. The surface of the trigone is smooth, and there the submucous layer is scanty and the mucous membrane is adherent to the subjacent muscular tissue.

The mucous membrane is continuous in front with that of the urethra, and behind with that of the ureters.

The exact nature of the glands which secrete the mucus of the bladder is not well settled as yet, but they are more like single racemose glands than anything else.

The bladder is provided with three arteries on each side, the upper, middle, and inferior. They are derived from the internal iliac.

The veins are specially abundant around the neck of the organ, where they form a marked plexus, the main formative branch of which is the dorsal vein of the penis.

The lymphatics open into the pelvic glands.

The nerves of the body of the bladder come from the sympathetic. Those of the base and neck come from the third and fourth sacral nerves.

The bladder is developed from the cloaca, *i.e.* the cavity formed by the terminal point of the primary intestinal cord and the pedicle of the allantois. In course of development there is thrown out a transverse partition which separates it from the rectum, and the pedicle of the allantois becomes obliterated and is then known as the urachus.

PECULIARITIES OF THE BLADDER.—The bladder is the largest of all the receptacles that are found in the course of the excretory apparatus of the body. It corresponds to the gall-bladder and to the seminal

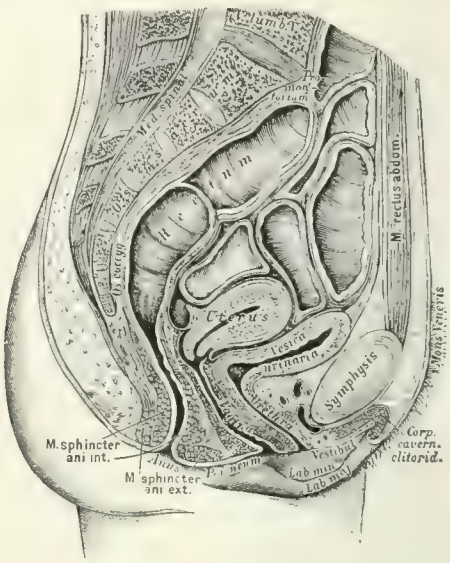

FIG. 648.—Sagittal Median Section through the Female Pelvis. About one-third natural size. (After Heitzmann).

vesicles. Together with the stomach it is the only organ that is susceptible of considerable enlargement within the bounds of health.

It encroaches upon two large cavities, the pelvis and abdomen. When empty it is flat against the pelvis. The difference of direction of the various axes is worthy of notice. The organ is as it were suspended by its two extremities, the neck and the urachus; but the neck is the less movable. The urachus recalls the pyramidal process of the thyroid

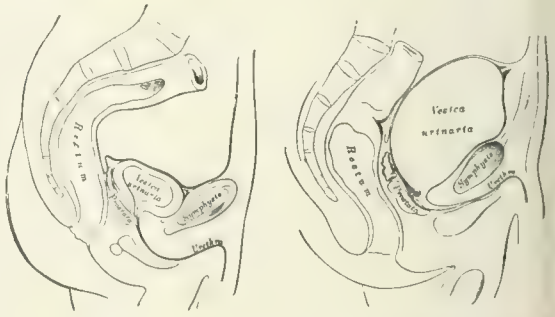

FIG. 649.—Median Sagittal Section through the Pelvis of a Young Man. A, bladder empty; B, bladder full. (Heitzmann.)

body. Upon close examination the bladder will be found to be really fusiform, the two pointed extremities corresponding to the apex or urachus and to the neck.

The absence of peritoneum on the anterior surface when the bladder is distended (see Fig. 649, B) is the reason why that surface is the spot chosen when it is desired to penetrate into the bladder. The relation of the base with the rectum makes the exploration by

way of the rectum indispensable in many bladder troubles. The presence of the urachus is noteworthy. The mode of attachment and the fixed character of the neck are evidently intended to direct the action of the fibers toward the orifice of the urethra.

The presence of three muscular coats is noticeable; so also is the triple origin of the longitudinal fibers, recalling the similar arrangement of the longitudinal fibers of the stomach. The sphincters formed by the outer fibers around the neck and around the orifices of the ureters are to be noticed. The bundle arrangement of the plexiform fibers is unique. The formation of alveoles on the mucous surface by the projection of these fibers is an arrangement worthy of notice.

The presence of the bas-fond, of the trigone, and of the slit-like orifices of the ureters is peculiar, and so also is the indistinct character of the glands of the mucous membrane. That a small organ like this should be provided with six arteries is remarkable, although it is true that the organ is hollow and that the arteries are small. The presence of an abundant venous plexus around the neck of the bladder is to be noted. That the body and the neck possess each a different nerve supply is also striking.

The development of the bladder in common with the rectum is to be remembered; and so also is its common development with the allantois. Arrest of development by which the partitioning of the bladder from the rectum does not take place accounts for those cases in which a cloaca persists into adult life. Failure of obliteration of the pedicle of the allantois explains the persistence of umbilical fistula. The fact that the bladder is developed separately from the urethra accounts for the cases of unperforated urethra in which the development is arrested before the proper time. The arrest of development before the abdominal wall is closed accounts for the cases of exstrophy of the bladder.

In fetal life the bladder is distinctly fusiform in shape.

Owing to the smallness of the pelvic cavity in the child the bladder encroaches at that age more on the abdominal cavity.

In old people the muscular fibers become more fibrous and the glands secrete more mucus.

The Female Bladder.—The bladder of the female differs from that of the male in size and relations. It is usually somewhat larger than the male bladder, with an excess of length in the transverse diameter.

The posterior surface is in relation with the uterus, separated from it by the fold of the peritoneum known as the vesicouterine cul-de-sac or pouch, excavatio vesicouterina [BNA].

The under surface or base has most important relations. It corresponds to the anterior wall of the vagina and to the lower third of the neck of the uterus. The ureters on the sides are close to the upper part of the neck of the uterus and the base of the bladder. These relations explain the occurrences of vesicovaginal and cervical fistulas. Edmond Souchon.

Bladder, Extirpation of the.—History.—The first operation for removal of the bladder was made by Bardenheuer, in 1887, in the male. The operation, through a subpubic incision, was incomplete, and the patient died on the fourteenth day. The first operation in the female was made by Pavlik, in 1888. Since that time more than a hundred cases have been operated upon. In this country the operation has been done by many different surgeons, both in the male and in the female. In the female, Martin of Chicago was the first to operate, his first operation being in 1892. The bladder was removed with a uterine fibroid. He has also operated on several other cases. Mann[1] of Buffalo operated on three cases, the first one in 1900. McCosh of New York performed the operation twice in 1903, once in a man and once in a woman. Frederick of Buffalo, Reynolds of Boston, Hartley of New York, and Lapthorn Smith of Montreal have each operated once. The operations upon the male for exstrophy have been quite numerous.

A bibliography of total cystectomy for tumors is given by Watson in the *Annals of Surgery*, xlii., 6, December, 1905. One of cystectomy for all causes is published by Verhoogen and DeGraeuwe in *Folia Urologica*, iii., 6, April, 1909.

Indications.—The indications for the performance of this operation are: first, incurable disease of the bladder, such as cancer and tuberculosis; second, exstrophy; third, incurable disease of surrounding organs which has begun to involve the bladder, such as cancer of the uterus in the female.

Management of the Ureters.—In the male the method generally proposed has been the grafting of the ureters into the bowel. In 100 cases collected by Bovée the ureter was grafted into the bowel separately 31 times; by the Maydl and Pozzi method, 44 times; into the urethra, 13 times; into the vagina, 8 times; and into the skin, 4 times. This is the most important question connected with the operation, and must be clearly understood. As the conditions in the male and the female vary very much, different methods may be used in the two sexes. I will, therefore, first consider the methods in the male.

The first plan used by Bardenheuer was to insert the cut ends of the ureters directly into the rectum. Experimentation upon the lower animals, by Peterson

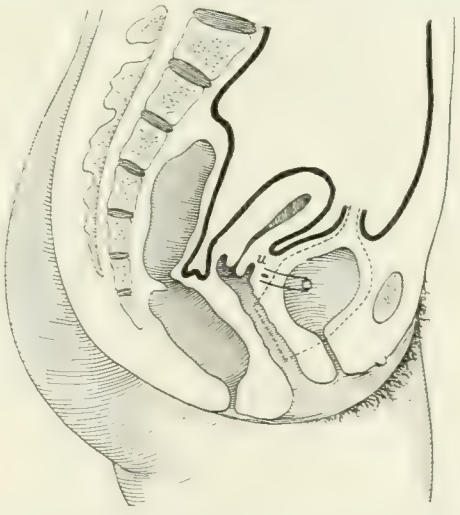

Fig. 650.—Extirpation of the Bladder. The dotted line shows the line of incision; the ureter (*u*) is roughly shown entering the bladder.

and others, shows conclusively that this is an exceedingly dangerous method, as in almost every case, within a comparatively short time, infection traveled from the bowel to the kidney, and the animal died of this complication. The same thing has been noted in man, and the method is now considered so dangerous as to be practically given up.

Maydl proposed the removal of the trigone of the bladder with the ureters, and the transplantation of this piece of the mucous membrane of the bladder directly into the intestine. The results of this have been very much better, as the natural valvular action at the end of the ureters seems to prevent the ingress of infecting germs; so that many cases in which this has been performed have been permanently successful. This can be done only in cases in which the trigone is healthy, so that in exstrophy of the bladder it is the recognized method. In the case of malignant disease and of tuberculous disease, which are most

apt to affect the posterior wall of the bladder, it may be impossible to dissect out the trigone; in which case it will be necessary to put the cut ends of the ureters into the intestine. But, as this is almost certainly fatal, it would seem to rule out operations for removal of the bladder for these indications in the male in a large proportion of cases.

In the female we have the choice of two methods, both of which have been proved to be successful. We may either open the ureters into the vagina by a previous operation, as was done by Pavlik, or we may leave the cut ends of the ureters opening into the vagina after the removal of the bladder—methods which really amount to the same; or we may perform the operation of Maydl, or, better still, its modification by Pozzi.

Pozzi's operation differs from Maydl's in that more of the mucous membrane of the bladder is removed, and the trigone is not retained in one piece, but is divided by making a longitudinal median incision before separation. The results of both the Maydl and Pozzi operations have been most satisfactory. Out of forty-four cases only two deaths occurred from infection.

The grafting of the ureter to the skin has been done ten times, but the results are not encouraging. Sonnenberg implanted the exposed ureter of an ectopic bladder into the urethra of the glans penis. In all, more than twelve cases have been done by this method. It leaves dribbling of urine, but this is more easily taken care of than in the case of grafting to the skin.

In the female, when the bladder is removed, by removing at the same time a portion of the anterior wall of the vagina the cut ends of the ureters may be left entirely alone; and, when cicatrization has taken place, they will be found to empty into the vagina. This gives an opportunity of making a receptacle for the urine out of the vagina by simply closing the vaginal entrance. As the urethra must also necessarily be cut in removing the bladder, it also will open into the vagina, and the patient will be able to empty the vagina through the urethra, either by the catheter or by voluntary effort, as was done in Pavlik's case. If the vagina is maintained in an aseptic condition during healing, ascending infection will be prevented. After complete healing of all the parts the danger of infection will be very greatly diminished.

In exstrophy of the bladder, in the female, the Maydl or the Pozzi operation may be done in the vagina, thus obviating the necessity of opening the abdomen.

The Mauclaire-Gersuny operation consists in implanting the ureters into the rectum, which is cut off from the bowel above after an artificial anus has been made. Gersuny modified the original operation by bringing the bowel exit into the sphincter ani, thus doing away with the artificial anus and maintaining a separate receptacle for the urine.

Technique. *Exstrophy in the Male.*—The trigone is first dissected out with the ureters. The abdomen is then opened and the trigone carried into the rectum through an incision and sewed in place. After this the bladder is removed and the opening closed. The incision may be made curved, with its concavity downward from one inguinal canal to the other; a vertical incision may be made which can be enlarged by a transverse incision crossing the lower end of the vertical one.

Exstrophy in the Female.—Here the Pozzi operation will be necessary, in order to get around the uterus. If it is desired to transplant the ureters into the vagina, a transverse incision may be made down to the peritoneum. After the trigone has been dissected out, the vagina can be pushed up by an assistant and opened and the trigone inserted. It will be necessary to dissect off the mucous membrane of the vagina on the anterior wall beforehand, so as to make a raw surface to which the trigone can adhere. The closure of the vagina can be left to a later date.

Cancer or Tuberculosis in the Male.—Although the indication may seem to be urgent, so far the technique of the operation is not complete enough to warrant its performance unless the parts around the bladder are healthy. This can be satisfactorily ascertained only after the bladder is opened. Suprapubic cystotomy must first be performed, and the bladder carefully examined. If the trigone be healthy, the abdomen must then be opened by a free longitudinal incision, the bladder thoroughly disinfected and laid open, and the trigone may then be dissected out (the patient being in the Trendelenburg position), with the ureters, and put into the rectum; after which the bladder may be easily removed, mostly by blunt dissection.

Cancer or Tuberculosis in the Female.—Owing to the fact that the ureters may be left undisturbed in the female, the operation is much easier than in the male. After the bladder has been carefully washed out, a median abdominal incision is made, and the patient put in the Trendelenburg position, self-retaining retractors being introduced. The peritoneal covering is then incised over the bladder from side to side. The bladder is afterward loosened with the finger down to the attachments of the base, so that it is held only by the urethra, ureters, and attachments to the anterior wall. These are then cut with strong scissors, so as to remove a portion of the anterior wall of the vagina as big as a fifty-cent piece. Any bleeding vessels are tied and the peritoneum closed over the seat of the bladder with catgut suture. If the patient be in good condition, and no previous infection of the bladder exists, the vaginal entrance may then be closed by a plastic operation.

After-treatment.—In order to keep the urine aseptic, and thus prevent ascending infection of the ureters, in all these operations it is well to give the patient large doses of benzoate of ammonium, beginning a few days before the operation. In women the vagina must be kept well cleansed out and drained. If the vagina be closed at the time of the operation, a self-retaining catheter should be passed through the urethra and left, the vagina being washed out through the catheter at least twice a day.

Results.—Bovée, in 1901, collected reports of 100 operations. Of these the operation was done sixty-eight times for exstrophy, twenty-one times for malignant disease, three times for tuberculosis, once for epispadias, once for fibroid of the uterus, and six times for conditions not noted.

For exstrophy Maydl's operation was done thirty-eight times, with eight deaths; Pozzi's operation, four times—no deaths; anastomosis of the ureters into the rectum, ten times, with three deaths; and separate anastomosis into sigmoid, twice, both patients dying. Sonnenberg's operation was done thirteen times—no deaths.

For malignant disease twenty-one operations were done, with eleven deaths. In seven the ureters were grafted into the vagina, with one death from collapse, and one from peritonitis on the ninth day.

For tuberculosis, three cases, with two deaths, are reported.

Altogether there were twenty-seven deaths in 100 cases. Sixty-eight operations for exstrophy gave nineteen per cent. mortality, and thirty-two operations for other conditions gave forty-two per cent. mortality.

Verhoogen and DeGraeuwe[2] collected reports of sixty-one cases, in fifty-nine of which the results were stated. There were thirty-one deaths, three immediately following the operation. Matthew D. Mann.

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1. Transactions Am. Gynecological Society, 1901.
2. Folia Urologica, iii. 6, April. 1909.

Bladder, Injuries and Diseases of the.—MALFORMATIONS.—The development of the bladder may be arrested at various stages in its progress. Occasionally the septum which divides the rectum from the bladder is wholly or partially wanting, so that they freely communicate with each other, or, in extreme cases, form together a large pouch (cloaca) into which the intestine and ureters open. This condition of things may be associated with imperforate anus. Entire absence of the bladder has been reported, in which case the ureters opened directly into the urethra.

Exstrophy.—The most common fault of development, however, is the absence of the anterior vesica wall. This deformity, known as exstrophy of the bladder, is far more common in males than in females. It consists in a failure of union of the two halves of the body along the abdominal surface. The anterior wall of the bladder, and the abdominal wall over it, are wanting, and the pubic bones are generally separated by a considerable interval. The posterior vesical wall is consequently exposed to the air, and is pressed forward by the intestines behind it, thus forming a prominent tumor which may reach the size of the palm of the hand. This bulging bladder wall, owing to the constant irritation to which it is subjected, is much reddened and inflamed, and is usually covered with stringy alkaline mucus. In the lower part of this protruding mass may be seen the openings of the ureters, which are revealed by the constant little jets of urine escaping from them. They are sometimes much dilated. The rudimentary penis, which is always in a condition of complete epispadias, usually exists merely as a slight prominence, but may be of considerable size. It sometimes even retains a considerable power of erection, a point to be considered in the fitting of an apparatus. In connection with exstrophy are associated not infrequently herniæ of one or both sides. In the female, exstrophy is generally complicated with prolapse or procidentia uteri.

FIG. 651.—Exstrophy of Bladder in a Girl of Sixteen Years. Complete exstrophy. Pubic rami are separated four inches, the position of the ends being approximately shown by the pubic hair. Above is the bulging posterior bladder wall, while below, the thickened hypertrophied cervix protrudes from the vulva. (Case of Dr. M. H. Richardson.)

If the fault of development is not so extensive as in complete exstrophy, the abdominal walls may unite entirely up to the umbilicus, which fails to close and leaves a fistulous communication with the bladder through the still patent urachus. An even lesser degree of the same deformity is represented by a prolongation of the bladder up into the lower portion of the urachus. Sometimes the canal may be shut off from the bladder and form a cyst, or a series of cysts.

The suffering in a case of complete exstrophy is usually very great.

The treatment may be briefly summarized under three heads:

FIG. 652.—Exstrophy of Bladder in a Boy of Five Years. Complete exstrophy. Penis rudimentary, showing condition of epispadias. Both testicles undescended and double inguinal hernia. Loose puckered skin below penis is the scrotum, and suggests the possibility of using it as a skin flap to cover the defect. (Case of Dr. C. B. Porter.)

I. Treatment by Apparatus.—This method is applicable to (1) All cases in which the defect is moderate and the condition of the patient is not sufficiently distressing to lead him to desire operation. (2) Cases in which plastic operations have been tried and have failed. (3) Cases in which the coexistence of other disease makes any operation inadvisable.

The rubber urinals manufactured for these cases are unsatisfactory, as they press upon and irritate the mucous membrane. The best apparatus is a silver or German silver shield, which arches over and protects the bladder, with a dependent portion into which the urine runs, and which communicates by a tube with a rubber bottle strapped against the leg. In order to get a well-fitting apparatus, it is a good plan to have first made a flexible, metallic ring, large enough to encircle the bladder. This is then bent and adapted to the inequalities of the surface, and, finally, the edge of the shield is fitted and soldered to it. The whole is held in place by a belt and perineal straps.

II. Treatment by Plastic Operations.—The utmost that we can reasonably expect to gain by any plastic operation for the relief of exstrophy is the greater comfort of the patient and greater ease in fitting apparatus. A truly retentive bladder cannot be obtained, and while the mortality of these operations is commonly sup-

posed to be insignificant, such is not the case, for the repeated attempts to obtain closure of the wounds seriously undermines these little patients' strength. Clearly brilliant results are not to be expected from operations of this kind. Plastic operations may be divided into two classes:

1. Those in which the skin of the abdomen is used in making the anterior bladder wall. The flaps may be taken from a variety of sources, but the most satisfactory is Wood's operation, by which a flap large enough to cover the defect is taken from above and turned down so that the skin surface is innermost, and stitched in position. The raw surface of this flap may be covered by flaps drawn over it from the sides by skin grafts, or left to granulate.

Fig. 653.—Apparatus for Palliative Treatment of Exstrophy. Above is shown the belt to go around the body, holding in place the metal shield of silver or German silver with a cup-shaped dependent portion into which the urine runs. On either side below are the perineal straps which fasten to the belt behind, and between them is the tube connecting the shield with the rubber receiving bottle fastened to the leg.

The objections to all operations in which the skin is used to restore the defect are the great tendency to calculus formation and the danger of irritation from hair growing into the bladder.

2. Those in which the mucous membrane alone is utilized. These operations depend on the possibility of getting enough mucous membrane to make a continuous canal from the openings of the ureters to the base of the penis. The urethra is then restored by an operation for epispadias, and thus in some cases the problem of fitting a urinal may be greatly simplified and the discomfort of the patient proportionately lessened. In selected cases this is an excellent procedure.

III. Radical Cure by Implantation of the Ureters into the Bowel.—The unsatisfactory results obtained by plastic operations and the discomfort incident to all forms of apparatus have led to attempts at radical cure of the condition by the removal of all that remains of the bladder wall and suturing the ureters into the bowel. The advantage of such an operation is the entire relief from the discomforts incident to the condition. The bowel soon becomes accustomed to its new function and the urine is passed at intervals closely approaching the normal. The dangers are twofold: those arising from the immediate effects of the operation and those resulting from infection of the kidneys by intestinal bacteria. The immediate mortality of the operation is by no means small, and though the statistics on the subject are too meagre to warrant a definite opinion, it is probably not far from that of other operations involving resection of the bowel. The more remote effects are those resulting from infection of the kidneys, and it is upon this issue that the ultimate value of the operation must be decided.

We are still somewhat in the dark as to the conditions which influence infection of the kidney under these conditions. Considerable doubt has been shed upon the older view that protection of the kidney was due to the anatomical arrangement by which the ureters enter the bladder obliquely. It is now very generally believed that the circular fibers in the wall of the ureter itself play an important part in preventing reflux from the bladder. Whatever may be the importance of the protective mechanism the fact remains that operations involving transplantation of the ureter, particularly into the bowel, have been exceedingly likely to be followed by pyelitis and pyelonephritis. No method has as yet been devised which will certainly avoid this danger, which is therefore a serious menace to the ultimate success of the operation. Though a number of operations of this type have been devised, and a good many cases are on record, no considerable number of brilliant results has been recorded and such procedures cannot be advised with enthusiasm. Children who will later be obliged to work, and adults who are competent to decide the question for themselves, would seem to be the most favorable subjects for this operation.

The limits of this paper will not permit of an extended discussion of the various forms of operation that have been proposed, for as yet no one method has attained a stable position. [See also the article on *Extirpation of the Bladder*, page 70.]

Diverticulum.—Another type of malformation generally believed to be due to defective development is the so-called diverticulum of the bladder. This consists of sacculations involving all the coats of the bladder and having a small orifice, though the cavity may be of considerable size even equalling the capacity of the bladder itself. They may occur in any portion of the bladder wall but are most frequently seen in the neighborhood of the ureteral orifices, often to the outer side. On account of this location it not uncommonly occurs that the orifice of the ureter is drawn into the diverticulum to such an extent as to be inaccessible. These sacculations are important for two reasons. First, because when they exist in the neighborhood of the ureter they generally involve that structure in pressure and ultimately produce dilatation of the ureter and compression atrophy of the kidney. The second way in which they become a menace is through infection, for they are commonly the seat of residual urine and should infection occur the cystitis, so called, becomes very intractable. They may exist in considerable numbers scattered over various portions of the bladder wall and when numerous are likely to be small. Their discovery is frequently quite accidental, coming about during the investigation of the cause of pus in the urine or in the cystoscopic examination of the bladder for some other cause. Since they are undoubtedly a menace to the integrity of the kidney as well as to the proper emptying of the bladder, they should be removed by operation whenever possible.

Hernia of the Bladder.—This displacement may be congenital or acquired. Like other herniæ, it is sometimes brought about by violence or over-exertion. It may appear at any of the orifices in the lower

abdomen through which other hernia occur. The most common forms are inguinal in men, and vaginal or femoral in women. The hernial sac usually contains also portions of intestine and omentum, but may be occupied by a part of the bladder alone. The portion of the bladder in the sac is usually not covered by peritoneum, although exceptionally it may be. The presence of the bladder in a hernial sac is sometimes brought about by its adhesion to the intestine or omentum, which then drags it down with it.

The *diagnosis* is to be made by the aid of the catheter, the tumor being emptied when the urine is drawn from the bladder. Pressure on the tumor, too, hastens the flow of the urine.

The *treatment* of hernia of the bladder is essentially that of hernia of other viscera except in so far as its existence brings with it additional dangers if treated palliatively—namely, those incident to the presence of cystitis; for inflammation may occur in a sacculation as the result of stagnation and consequent fermentation of the urine. Unless some concomitant disease forms a distinct contraindication, an attempt should be made to cure the condition by radical operation. If this cannot be done, the sac should be supported by a pressure bandage, and the escape of urine should be aided by pressure during micturition. If, in spite of these precautions, the bladder is still incompletely emptied, the dangers arising from the constant presence of residual urine may to some extent be obviated by the routine use of the catheter, emptying the bladder at least once a day, preferably in the evening.

Wounds of the Bladder.—The protected situation of the bladder renders it little liable to injury. In fracture of the pelvis, a sharp point or fragment of bone may penetrate its wall, or it may be injured by gunshot wounds, or by puncture with a sharp instrument. The treatment of this class of cases will be considered more at length under Rupture of the Bladder. The bladder may also be wounded by the unskilful use of instruments in lithotrity, or may be incised by accident during abdominal operation. In this latter case, if at once carefully stitched up, the wound usually heals without serious trouble.

The question of the advisability of closing openings in the bladder intentionally made, as in suprapubic lithotomy, must be decided in each individual case according to circumstances. While the ideal procedure is to close the bladder by immediate suture, the patient is often subjected to fewer risks if the wound is left open. The question must be decided by taking into consideration the general condition of the patient, the local condition of the bladder, and the trauma to which the bladder walls have been subjected during the operation.

Rupture of the Bladder.—Ruptures of the bladder are either idiopathic or traumatic. According to their location, they may be also classed as intraperitoneal and extraperitoneal. Among the extraperitoneal are to be reckoned the partial and the subperitoneal.

Idiopathic ruptures probably always occur in bladders altered by disease. A long-continued obstruction to the passage of the urine, as from a stricture or enlarged prostate, favors the formation of little herniæ of the mucous membrane through the meshes of the muscular tunic, and an over-violent strain duing some exertion, or in the effort to empty the bladder, may rupture one of these little thin diverticula. The vesical wall is also sometimes weakened by ulceration, simple or malignant, and is thus rendered especially liable to give way. During labor, the distended bladder may be ruptured by compression between the abdominal wall and some part of the child or instrument used in the birth. The rent in this case may be to into either the vagina or the peritoneal cavity.

Rupture of the healthy bladder is rarely produced, except by external violence in the form of a blow or crush. Probably it is sometimes also brought about by great muscular exertion when the bladder is distended, even though it be healthy. In traumatic ruptures, the bladder is almost always full at the time of the traumatism.

Great violence to the hypogastrium is capable of producing a tear in the anterior wall of an empty bladder. This accident is to be explained as follows: The force applied to the hypogastrium carries the upper portion of the bladder, which is attached to the abdominal wall by the peritoneum and urachus, violently backward. The lower part of the bladder is held by the prostate, which is fixed by the pelvic fasciæ, and consequently a rent occurs in the anterior vesical wall just above the prostate. This is often accompanied by a considerable stripping up of the peritoneum. Intraperitoneal rupture uncomplicated can occur only when the bladder is full.

Symptoms.—When a rupture occurs a feeling of giving way or of a tear is often experienced. If the bladder has been painfully stretched by long retention, the first feeling may be of relief. Soon, however, pain follows, and is referred to the whole abdomen or to the pelvic region. This is followed in the majority of cases by shock and inability to walk. There may be desire, but want of ability, to micturate. Catheterism is usually easy, but obtains only a little bloody urine; not infrequently, on pushing the catheter further, a "second escape" of fluid is obtained.

Many of these symptoms may, however, be wanting. The pain is sometimes not very great; micturition may be possible, though even then usually difficult. The catheter may draw clear urine.

The principles of treatment in rupture of the bladder may be summarized by the following rules:

1. When an intraperitoneal rupture is made out, an immediate laparotomy, with suture of the bladder wound and subsequent drainage of the bladder, should be done.
2. When a reasonable doubt exists as to whether the rupture is intraperitoneal or not, an immediate laparotomy should be done.
3. If an extraperitoneal rupture is made out, and uncertainty exists as to the direction in which the urine is extravasated, a laparotomy should be done for exploration to ascertain how the drainage may best be placed.
4. In the case of fracture of the pubes, with evidence that urine is extravasated in the prevesical space, an incision should be made in the suprapubic region, and a tube should be carried to the bottom of the effusion.

In short, a laparotomy should be done in all cases of bladder rupture except in those which come under Rule 4, or those of such severity that they cannot bear more than the median operation.

Tumors of the Bladder.—Tumors of the bladder may be classified as follows, in the order of their frequency: Papilloma, carcinoma (carcinoma papillosum, epithelioma), myoma, fibroma, sarcoma.

Papillary tumors form more than half all new growths of the bladder. They are made up of very vascular branching papillæ, clothed with irregularly cylindrical epithelium. They are either pedunculated or sessile, single or multiple, and upon their character in this respect depends the difficulty of their removal. Their favorite seat is in the neighborhood of the trigonum, and they may attain the size of a pigeon's egg, or even larger.

They give rise to intermittent hematuria, but generally there is no pain in the early stages. Pain usually appears later, however, and may finally become quite constant and severe, but should always raise the suspicion that the tumor is malignant in character and that the pain is due to involvement of pelvic

lymph glands. Occasionally, by their pressure, they cause obstruction to micturition or to the entrance of the urine through the ureters. Finally, cystitis is usually associated with them. The hematuria may, however, exist for a number of years before other symptoms appear. Although benignant in their character, they may finally cause death by the changes that they bring in their train. No method has yet been discovered by which the benign papillary growths can be distinguished from the malignant growths of similar gross appearance except by a microscopic examination of the base of the tumor. The view has been widely held that the benign tumors ultimately take on a malignant degeneration, but the demonstration of this fact is by no means complete and it is more likely that the cases ultimately proving malignant were cancerous from the start. The impossibility of drawing a distinction by observation alone makes it wise to regard all tumors of the bladder as potentially malignant.

The diagnosis can be made with certainty only by the aid of the cystoscope. With modern instruments, in skilled hands, failure to get a satisfactory view of the tumor is a rare occurrence. By this means it is possible to ascertain the general appearance, size, and position of the tumor, but in the papillary forms of growth it is not possible to say with certainty whether the tumor is malignant or benign.

Two methods of treatment are available, one of recent origin by means of the high frequency current, the other by removal of the growth through a suprapubic incision. Too little time has elapsed since the introduction of the high frequency current for this purpose to admit of an accurate estimate of its final place in treatment. At present, however, it seems to be a satisfactory method for treating small, apparently benign, growths, for multiple small tumors and for multiple recurrences after radical operation. The procedure is a simple one and can be carried out in the office. It consists in the introduction of a wire through the catheter channel of a catheterizing cystoscope and the direct application of the high frequency current to the tumor by means of this cable. Growths rapidly shrivel up and disappear, partly by actual destruction and partly by sloughing. Small growths may be destroyed at one sitting while larger ones may take several applications, best made at an interval of about a week. The operation is free from pain and discomfort other than that incident to cystoscopy.

The other method of dealing with these growths is by suprapubic operation. This method should be applied to all cases in which the use of the high frequency current is not indicated and to all cases in which doubt exists as to the character of the tumor. The operation should be truly radical and should remove the whole thickness of the bladder wall with a considerable margin around the base of the tumor, which should be handled as delicately as possible to avoid scattering its cells and producing implantation growths. Since the transperitoneal operation gives the best access to these tumors it is generally to be preferred.

Primary carcinoma of the bladder occurs either in the form of papillary cancer, in which an indurated cancerous base is covered by papillæ resembling those of the simple papilloma, or as an epitheliomatous ulcer with hard indurated base and edges. Scirrhus is rarely met with, as is also an encephaloid form of the disease.

The symptoms resemble those of papilloma, but are sooner or later associated with severe lancinating pains in the bladder and its neighborhood. The cancerous cachexia is often very marked.

These tumors show a very marked tendency to late metastasis which has encouraged the attempts at their radical removal. Where they grow upon the vertex or lateral walls of the bladder there is considerable chance of success and radical operation should be advised. It should consist in a wide removal of the whole thickness of the bladder wall and if necessary a portion of the ureter when this is involved in the growth. The ureter when thus divided should be reimplanted into the bladder wall higher up. Growths which involve the trigonal portion of the bladder are frequently impossible of removal owing to infiltration of the perirectal and periprostatic tissues and to their greater inaccessibility.

The operation of total cystectomy for cancer has not as yet reached a stable position owing to the difficulty of satisfactorily disposing of the urinary stream. Implantation of the ureters into the intestine, vagina in the female, or the skin, either exposes the patients to a very large danger of renal infection or leaves them in a condition not notably more comfortable than their previous one. The operation of Watson consisting of a double lumbar nephrostomy with ligation of both ureters and then extirpation of the bladder at a second operation seems the most feasible procedure.

In less promising cases much relief may be afforded the patient by suprapubic cystotomy and curetting the growth. This procedure may be repeated if necessary, and may decrease the suffering and lengthen the life of the patient considerably. Death ultimately takes place from generalization of the disease with symptoms which vary according to the organs implicated, the liver being almost invariably the seat of secondary deposits.

The *myomata* and *fibromata* can hardly be considered separately, as they usually occur in a mixed form, myofibroma or fibromyoma containing both fibrous and muscular elements. They are very rare. Gussenbauer, Volkmann, and A. T. Cabot have removed tumors of this character. Gussenbauer's and Cabot's patients recovered, while Volkmann's died. Tumors of this class may give rise to symptoms of obstruction, but do not as a rule cause hematuria or cystitis.

A. T. Cabot has called attention to the condition known as *pachydermia vesicæ*, in which the mucous membrane of the bladder is changed into a membrane consisting of epidermoid cells. The relation to carcinoma appears to be close, and in the case reported (*American Journal of the Medical Sciences*, February, 1891) death ultimately occurred from that cause.

Primary sarcoma is extremely rare. Tumors of the prostate and bladder secondary to a round-celled sarcoma of the testis have been mistaken for primary sarcoma.

Besides the regular tumors mentioned above, *cysts* may rarely occur. They are sometimes congenital and contain hair, bones, etc.

Neurosis of the Bladder.—Spasm of the bladder, when not due to inflammation, is probably in the great majority of cases dependent upon an increased sensibility of the prostatic urethra, causing by reflex action an excessive contraction of the detrusor urinæ muscle (see *Prostate, Diseases of the*).

In this connection we may mention the retention of urine which not uncommonly follows surgical operations, especially those involving the region of the perineum. It is due apparently to a reflex inhibition, the stimuli starting from the seat of the operation. This condition can often be relieved by the use of hot applications to the hypogastrium or perineum, and in women by spraying the vulva with warm water. If, however, all efforts to induce the patient to pass urine fail, the catheter must be used before the distention of the bladder becomes extreme, and when once started the use of the catheter may have to be continued for several days before the power of voluntary micturition returns.

Paralysis of the bladder is usually consequent upon some disease or injury to the nervous system.

The lesion may exist in peripheral nerve trunks, or may be located either in the reflex or in the motor center (spinal cord or brain).

The loss of power may be total or partial. When the paralysis is complete (which occurs usually in connection with paraplegia), the sphincters, both voluntary and involuntary, are also paralyzed, and after the accumulation of the urine produces a tension in the bladder great enough to overcome the resistance in the urethra, a leaking of the overflow commences. As sensation is lost in these cases the distention of the bladder and escape of the urine are often not perceived by the patient.

If the paralysis comes on slowly, as it may do in cases of spinal sclerosis, tabes dorsalis, and Pott's disease, it first makes itself known by the diminution in the force of the stream, and the increase in the time occupied in urination. When the paralysis is extreme, the pressure of the abdominal muscles furnishes almost the only driving power, and the stream dribbles perpendicularly from the meatus.

As the act of urination becomes more and more incomplete the amount of residual urine slowly increases until finally the bladder becomes distended and the overflow begins to escape, either intermittently or constantly. In either case a partial power of urination may be preserved. When the distention becomes extreme, the pressure is transmitted back to the kidneys, and may be so great as to cause suppression of the urine and uremia.

Besides this true paralysis, dependent on nervous lesions, there is also occasionally a partial or temporary loss of power, dependent upon general disturbances of the nervous system, such as hysteria, nervous prostration, and the debility following sexual excesses.

Atony of the bladder, by which is understood a weakness or loss of contractile power of the muscular coat, is not infrequently seen as a result of overstretching, which may be brought about by voluntary retention, or may be the result of obstruction in the prostate or urethra. It is considered in this connection, not because it is due to any nerve lesion, but because the local condition and its treatment are closely allied to those of paralysis. The condition is closely analogous to the enfeebled condition induced in any voluntary muscle which is persistently kept upon the stretch.

The diagnosis of paralysis or of atony of the bladder, when existing in any marked degree, is usually not difficult, although sometimes the constant escape of urine from an overfilled bladder leads to the erroneous idea that true incontinence exists. This mistake will be avoided by an examination of the hypogastrium, where the bladder, if full, will be easily detected. Any doubt as to the character of a central tumor above the pubes should lead to the passage of a catheter.

Atony of the bladder, if dependent upon some condition that can be relieved, may be recovered from. The chance of a favorable termination is, however, much more doubtful in old and worn-out subjects.

True paralysis occasionally depends upon some nerve lesion (meningitis, apoplexy, syphilitic inflammation, fracture of spinal column), which admits of more or less complete recovery. In the majority of cases, however, the loss of power is permanent. The cystitis, which is its most uncomfortable accompaniment, may be kept under control by proper care.

The treatment in cases of paralysis and atony should consist, first, in the systematic use of a catheter. The bladder ought to be emptied at least as often as once in the twenty-four hours when the loss of power is partial, while in complete paralysis this should be done four or five times a day. In addition to this, irrigation should be regularly employed, especially when cystitis has already started. If the loss of power is partial, the washing may be done with cold solutions, which have a stimulating influence upon the detrusor muscle. The systematic use of urotropin in doses of gr. v. to x., three times a day, appears to have a distinct influence in postponing the advent of cystitis and in rendering it less severe. Cold bathing of the abdomen and sacral region may also be useful.

Electricity is sometimes used with advantage. One electrode should be placed over the sacrum, and the other just above the symphysis pubis, in the perineum, or within the bladder itself.

Besides these local measures of treatment, the strength of the patient should be supported as far as possible by regulation of the diet, by exercise, and even by change of climate if it seem wise.

Strychnine and ergot are both thought to have a beneficial effect upon the muscular wall of the bladder, and general tonics are of use by their effect upon the general system.

When the power of retention is lost, a urinal becomes a necessity.

Inflammation of the Bladder (Cystitis).—Of recent years a very considerable change has taken place in our conceptions of the condition known as cystitis and we have come to recognize that, except in unusual cases, it is a symptom of some other condition and not a disease in itself. This change of view has come with the more thorough, and consequently satisfactory, investigations of the urinary tract in both sexes, due to the more extended use of the cystoscope and ureter catheter. We have come to recognize that the bladder is far more resistant to infection than many other portions of the urinary and genital apparatus with which it is anatomically associated and that its inflammations are as a rule of secondary and not of primary occurrence. It may reasonably be doubted whether cystitis, meaning a pure inflammation of the bladder mucous membrane not associated with disease of other portions of the genital or urinary mechanisms, ever occurs. One by one the cases of acute cystitis or chronic cystitis, supposed to be due to conditions arising within the bladder, have been shown to be of secondary nature and the only doubtful cases are those of so-called acute cystitis occurring in young women. I am confident that most of these will prove to be secondary and generally merely symptoms of acute pyelitis.

Etiology.—We shall perhaps make the matter clearer by enumerating briefly the conditions with which inflammations of the bladder are associated in a secondary capacity. Infections of the kidney and ureter, whether primary or due to calculus, frequently result in the symptoms of cystitis and less commonly in actual inflammation of the bladder mucous membrane. As an instance of this may be cited the very irritable bladders seen in early cases of renal tuberculosis in which the bladder itself does not as yet participate but which are still unfortunately commonly regarded as cases of cystitis. Inflammations of the prostate, acute or chronic, and stricture of the urethra of any origin frequently give rise to the symptoms and sometimes the signs, of cystitis, and the commonest cause of true cystitis is the obstructive lesions occurring in the prostate in later life. Changes in the bladder itself, notably tumor, diverticulum, and stone, not secondary to prostatic obstruction, may result in cystitis. Lesions of the pelvic viscera in both sexes are often the primary cause of trouble. Inflammatory lesions of the tube or ovary, tumors of ovarian or uterine origin, inflammation of the sigmoid flexure, generally due to diverticulitis, and inflammation of the perirectal tissue, are common instances.

All the above enumerated conditions act in preparing the soil of which the later cystitis is the result. They must, therefore, be regarded as the primary cause and attention must be addressed to their relief if a satisfactory understanding of the cystitis is to result. Given the prepared soil the necessary

infecting organisms will not be long wanting but without it they are quite unable to gain a foothold.

There are five routes by which bacteria may reach the bladder: (1) By the urine from the kidneys; (2) through the urethra on instruments; (3) through the blood; (4) from the rectum and sigmoid flexure, either by passing through the peritoneum or through retroperitoneal lymphatics; (5) by direct extension from adjoining areas of suppuration, *e.g.* infected urethra, prostate, or pelvic abscess.

A discussion of the comparative frequency of these various sources of infection would exceed the limits of this paper, but a few interesting observations may be noted.

Posner and Lewin found that after ligation of the rectum in animals, intestinal bacteria soon appeared in the urine and disappeared when the ligature was removed. Werden succeeded in producing cystitis by causing an artificial retention and making an abrasion on the rectal mucous membrane.

The constant presence of the typhoid bacillus in the urine of typhoid fever is now generally accepted and is doubtless the cause of many of the cases of cystitis occurring in this disease; but the discovery is even more valuable as suggesting the possibility that a similar condition exists in other acute infectious diseases, as the acute exanthemata, acute polyarthritis, etc., with the bacteriology of which we are less familiar.

The bacteria most commonly found in cystitis are: (1) The group of bacteria of which the bacillus coli communis is the type and which are found in more than one-half of all cases of cystitis. (2) The proteus vulgaris of Hauser, a common intestinal saprophyte. (3) The staphylococcus aureus, albus, and citreus. (5) The streptococcus pyogenes. (5) The tubercle bacillus.

All of the above-mentioned bacteria are capable, under favorable circumstances, of decomposing urea, but the colon group and the tubercle bacilli do so much less rapidly, and in the cases in which they occur the urine is more likely to be found acid.

In rare instances the gonococcus causes a true cystitis.

Pathology.—The pathological appearances vary with the severity of the inflammation. In simple catarrhal cystitis, the mucous membrane is more or less swollen and reddened, with the minute vessels sometimes visibly injected. This redness is usually most marked on the summits of the folds or rugæ, which may be studded with punctate hemorrhages if the inflammation has been of considerable intensity. Streaks of viscid mucus cover to a greater or lesser degree the inflamed surfaces. These appearances may be confined to the neighborhood of the urethral opening (partial catarrh, catarrh of the neck of the bladder), or may be diffused over the whole mucous membrane (universal catarrh). Even in this latter case, however, the evidences of inflammation are usually most marked about the urethra and trigone.

A loss of the superficial epithelium (erosion) sometimes occurs, and this is occasionally associated with the formation of false membrane (croupous inflammation). A severe inflammation sometimes leads to ulceration which may be diphtheritic in character. Rarely sloughing of considerable portions of the mucous membrane, and also of the muscular coat, follows long retention. When inflammation extends to the deeper layers of the bladder, the tissues are much thickened and infiltrated with pus, which may lead to the formation of abscesses. These may extend outward through the surrounding cellular tissue, and open spontaneously into the vagina, rectum, neighboring coil of intestine, or into the peritoneal cavity. Occasionally, however, they perforate the mucous membrane, and open into the bladder itself.

Dr. Samuel Alexander has described a condition known as nodular or follicular cystitis. It is characterized by intense congestion and the appearance, especially in the region of the trigonum, of hyperplasia of lymph nodes, somewhat resembling the condition of the ileum in typhoid fever.

A long-standing catarrh causes a brown or gray discoloration of the mucous membrane, often with considerable dilatation of the veins, especially about the urethral opening. The surface is covered with mucopus which is often extremely viscid and adherent. The mucous membrane and parts beneath are much thickened and infiltrated. If an obstruction has been the primary cause of trouble, the muscular coat of the bladder is greatly hypertrophied and forms interlacing bands which stand out like the columnæ carneæ of the heart (*vessie à colonne*). At the same time that the bladder is thus thickened, it is often also dilated (eccentric hypertrophy). Little herniæ of the mucous membrane, between the fibers of the muscular coat, are not infrequent. Lastly, inflammation of the bladder may be tuberculous in character, in which case the mucous membrane of the bladder, the prostate, ureters, and even the pelves of the kidneys may be the seat of characteristic ulcerations.

Clinical History.—In cystitis the most prominent, almost unfailing, symptom is a *frequent desire to urinate.* This varies greatly in degree, from a slightly increased frequency of micturition which escapes notice, to an almost constant, painful tenesmus of the bladder, compelling straining efforts which accomplish only the voiding of a few drops at a time. It must, however, always be remembered that these symptoms are by no means characteristic of cystitis and except in their most severe manifestations may occur in lesions of the kidney or prostate without any involvement of the bladder itself. The symptom next in importance is *pain.* This may be very slight, and felt only just before and at the end of micturition. It may, however, be almost constant and severe in character. The pain is ordinarily referred either to the hypogastrium, the perineum, or the end of the penis, but when severe assumes a lancinating character, shooting down the thighs, through the lumbar and sacral regions, and to the testicles. Pain referred to the hypogastrium, especially if accompanied by tenderness in that region, is usually indicative of inflammation affecting the body of the bladder. When the neck of the bladder is especially affected, the pain is referred to the perineum and to the end of the penis. These two prominent symptoms are usually accompanied by some *fever* in cases of acute universal cystitis. In inflammation of the neck of the bladder fever may be present, but is often slight or entirely wanting. In chronic cystitis there is ordinarily no febrile reaction. *Retention of urine* occurs rarely as a complication; it is most common in cystitis following gonorrhea, when a deep urethritis exists, and it is then due to a spasmodic contraction of the constrictor urethræ muscle.

Constipation is almost always present, and not only do the difficult movements of the bowels greatly aggravate the pain in the bladder, but experiments would suggest that the condition may favor a fresh supply of infectious organisms from the intestine.

Cases of chronic cystitis, dependent upon conditions which cannot be removed, run a protracted course with many ups and downs. Errors in diet, exposure to cold, over-exercise, or any excess in alcoholic liquors or in sexual excitement, bring fresh accessions of inflammation, which are recovered from with ever-increasing difficulty, especially at an advanced age. Finally, some serious complication, such as inflammation of the pelvis and secreting portion of the kidney, ulceration, possibly diphtheritic, of the bladder wall, formation of an abscess, septicemia or uremia, appears and quickly closes the scene.

The character of the urine is of great importance in supplying information as to the condition of the bladder. In a mild case, the urine may be acid and but

slightly cloudy. When the urine is allowed to stand for some time a light sediment separates, consisting of muco-pus, with usually a considerable number of flat epithelial cells. As the cystitis increases in severity, the urine becomes more and more turbid from the increasing amount of pus; and in addition to the squamous surface epithelium, rounded cells, derived from the deeper layers of the bladder mucous membrane and from the prostatic urethra, make their appearance. If, finally, alkaline fermentation occurs, the urine acquires a pungent ammoniacal smell, and the pus assumes a thick ropy consistency. Bacteria are also present in great number, giving a cloudy appearance to the urine even after the pus has settled out of it. Strongly ammoniacal urine causes the pus cells to swell to several times their natural size, and finally to dissolve. Casts, if present, are similarly dissolved, a fact which should be borne in mind when examining for evidence of coincident kidney disease. Blood corpuscles may be present in cases of cystitis of some severity, but in ammoniacal urine are quickly dissolved. The blood-pigment in this case imparts a brown or smoky color to the urine, which is quite characteristic.

Occasionally blood in considerable quantities may be passed and easily recognized. Besides these cellular elements many crystals are found in the urine of cystitis. In strongly acid urine, crystals of uric acid or oxalate of lime are not infrequent. If they are in considerable quantity, and especially if of large size, they may be suspected as the possible predisposing cause of the inflammation. In ammoniacal urine, the crystals usually found are those of triple phosphate and urate of ammonia, with which are often associated amorphous phosphates in a finely granular form. If the bladder inflammation takes on a diphtheritic character, bits of discolored diphtheritic membrane may appear in the urine. Gangrenous inflammation of the bladder wall, which is usually the result of severe injury, long-continued pressure, or the breaking down of a new growth, gives the urine an excessively fetid character. The admixture of blood more or less decomposed gives it a brownish, smoky, or green color, and the sediment contains much granular matter and large granular corpuscles, besides the various cells and crystals found in severe cystitis. Occasionally, especially as a result of long-continued pressure, considerable portions of the mucous membrane are thrown off, and may be recognized as such in the sediment. In the case of a sloughing new growth, characteristic forms (villi) can frequently be found under the microscope.

Interstitial (parenchymatous) cystitis causes a train of symptoms much more severe than those occasioned by a simple catarrhal inflammation. There is ordinarily high fever, sometimes accompanied by chills. The inflammatory infiltration of the bladder walls stiffens them, and by hindering their contractions makes complete expulsion of the urine impossible. The ureters, or the urethra, may be obstructed by abscesses, or by inflammatory swelling about the orifices. If an abscess breaks into the bladder, the appearance of a greatly increased quantity of pus in the urine is followed by a decided improvement in symptoms. If the opening takes place into the intestine, the symptoms also improve, although they may speedily resume their serious character if the intestinal contents get into and infect the abscess cavity. If the pus finds its way into the perivesical connective tissue, it may work outward and point either above the pubes or in the perineum, in which case its approach to the surface is heralded by preceding edema and induration. Occasionally, perforation takes place into the peritoneal cavity, and speedy collapse and death is the consequence. Infiltration of urine is a very rare consequence of inflammatory rupture of the bladder wall, and its spread is limited by the attachment of the pelvic fascia along the brim of the pelvis. A localized pelvic abscess may thus be formed and require drainage.

Diagnosis.—When this article was last rewritten, only a few years ago, this section began as follows: "The diagnosis of a cystitis is usually a matter of tolerable ease, if the symptoms and condition of the urine are carefully inquired into."

How different is the condition to-day! We now know that the symptoms and condition of the urine rarely enable us to make a diagnosis of any accuracy and that a far more searching investigation must be instituted if we really desire the facts. This is of course due to our comprehension of the secondary nature of cystitis and of the necessity of finding the ultimate cause rather than of treating a result. In every case with the symptoms of frequency of urination, pain, and pyuria, a careful search must be made for the cause outside of the bladder itself. In acute cases it will frequently be impossible, or unwise, to institute the searching methods of examination which alone can give a result beyond dispute and if the condition subsides without going into the chronic stage a positive diagnosis may never be possible. We should, however, in all cases investigate as thoroughly as possible the condition of the structures, which are generally the cause of bladder irritability. In acute cases a careful examination of the renal regions should be made to elicit tenderness, particularly in the costovertebral angle which, if present, renders the diagnosis of acute pyelitis probable. The presence of fever, without demonstrable lesion other than in the bladder, should excite strong doubt as to the integrity of the kidney. If the case fails to clear up promptly radiographic plates should be taken to exclude a "silent stone" in the kidney or ureter as these are of by no means rare occurrence. In the male the prostate and urethra should be carefully looked over and in both sexes lesions of the rectum must be excluded. In the female, lesions of the pelvic viscera must be sought for, it being remembered that the sagging bladder floor in multiparous women not infrequently causes residual urine and conditions not unlike those resulting from prostatic obstruction in the male. Should the acute symptoms subside but the pus not disappear from the urine, a thorough study of the urinary tract must be undertaken. This should include cystoscopy, ureter catheterization, radiographic pictures, cultures, a search for the tubercle bacillus by stain and guinea-pig inoculation.

If the study of all cases of so-called cystitis be taken up in this way we shall come to a sounder realization of the truly secondary nature of the disease.

Prognosis.—Acute cystitis, when not dependent upon some previously existing chronic condition, may with proper care run its course in from two to three weeks. It is rarely severe enough seriously to threaten life.

Chronic cystitis, if dependent on some curable condition (stone, stricture, etc.), may be recovered from after the removal of the predisposing cause, provided that the long duration of the malady has not induced permanent organic changes in the bladder wall.

Advanced age and a weak constitution render the prognosis much less favorable. When the disease is the result of some condition which cannot be removed (enlarged prostate, tuberculosis, inoperable tumor, etc.), recovery cannot be expected, although a considerable amelioration of symptoms may be accomplished by appropriate and thorough treatment. The appearance of phlegmonous, diphtheritic, or gangrenous inflammation with or without the formation of abscesses, makes the prospect of recovery extremely doubtful.

Prophylaxis.—Many cases of cystitis could no doubt be avoided by intelligent care. Careful management of an acute gonorrhea, or of a stricture or enlarged prostate, would often enable the patient to escape the cystitis which they so frequently induce.

The most important prophylactic measure, however, is a thorough observance of aseptic precautions in any and all operative procedures upon the bladder. All metal and rubber instruments should be thoroughly cleaned and boiled immediately after using, and should then either be kept in an aseptic case or cleaned again immediately before using. The problem of cleaning gum elastic and webbing catheters is more difficult, and they can rarely be used with safety more than a few times. They should be cleaned with soap and water to remove the oil and then washed carefully with corrosive sublimate 1 to 1,000. The use of formaldehyde vapor generated in various ways for the sterilization of instruments that cannot be satisfactorily boiled, is a safe method *if* a method is employed which insures the vapor passing through the lumen of the instrument.

In all cases in which there is any doubt as to the healthy condition of the urethra it is wise to give it a preliminary washing with some mild antiseptic, and in cases in which urethritis exists, it is well to repeat this after the use of any instrument.

Of the great variety of lubricants one should be selected which is aseptic and non-irritant. Most of the antiseptic lubricants, and especially those containing carbolic acid or eucalyptus oil, are irritating. The undesirable effect of greasy lubricants upon rubber instruments has led to their displacement by the newer lubricants prepared from Iceland moss. Of these there are a great variety, good, bad, and indifferent and one should be selected which does not tend to cake or harden but maintains an even consistency, even though kept a considerable time. They are a great improvement over the lubricants previously used.

Treatment.—In acute cystitis, whether universal or partial, the thing of first and greatest importance is rest. Rest should be absolute in bed, in a horizontal position, or with the hips slightly raised. The bladder, irritated and intolerant of its contents, should be soothed by full doses of some anodyne to lessen as much as possible its overexcitability, and to quiet its constant spasmodic activity. The anodyne may be administered in the form of a suppository, a favorite combination being opium or morphine, with either hyoscyamus or belladonna. Not infrequently, however, it will be found wise to give the anodyne by the mouth, as rectal absorption is slow and sometimes unsatisfactory. If the pain is due mainly to the spasmodic action of the bladder, hyoscyamus or belladonna sometimes suffices to relieve it, and when either of these is efficient it is preferable to opium, which is objectionable from its constipating properties, even when it does not disagree with the stomach. Codeine will also be found useful, especially in the less severe cases. If, however, hyoscyamus, belladonna, or codeine does not control the pain, opiates should at once be resorted to; and these should be given in full doses, as a really curative effect is to be expected from the relief of spasm.

Heat, wet or dry, over the hypogastrium and perineum will often be of use, and if well applied will accomplish more than a hot hip-bath, which is commonly used, but which has only a transient effect. A hip-bath, if given, should be very hot, and the patient should be in it but a few minutes (four or five at the outside), as the necessary position, if maintained for any length of time, favors congestion of the pelvic organs, and to a great extent counteracts the otherwise good effects of the heat.

Medicinal treatment intended to modify the condition of the urine may be beneficial in two ways: first, by increasing the amount and consequently diluting the urine; and, second, by affecting its reaction and rendering it a less favorable medium for the growth of bacteria.

The most simple and generally an efficient method of increasing the amount of urine is to urge the patient to drink at least two quarts of water or milk in the twenty-four hours; if more can be taken, so much the better. To this may be added cream of tartar water, or citrate of potassium, both of which are mild diuretics and tend to stimulate the action of the kidneys. In this way the amount of urine can generally be kept sufficiently large markedly to dilute it. The vegetable diuretics, buchu, triticum repens, uva ursi, etc., are less used now than formerly, and they are not notably more efficient than the milder measures above mentioned.

Of the drugs which owe their power to the fact that they are excreted in some form in the urine, benzoate of sodium, boric acid, sandalwood oil, and many new compounds containing formalin are the most valuable. If the urine is ammoniacal, as is not infrequently the case, its irritating properties are thereby much increased, and the use of some drug to render the urine acid is distinctly indicated. The most efficient are benzoate of sodium and boric acid in doses of from gr. v. to x. every three to four hours, according to the reaction of the urine and the tolerance of the patient. Sandalwood oil has a soothing effect, especially when the inflammation is most marked about the neck of the bladder, but it is taken with difficulty by some patients and should always be given in capsules.

Besides this strictly medicinal treatment, the diet should be carefully regulated, only bland, unirritating articles of food being allowed. Alcohol in every form should be interdicted, and tea and coffee should be avoided or taken very much diluted. The bowels are to be kept gently open, and especial care in this direction is needed when opiates are being used.

When the inflammatory process is being combated in this manner, the predisposing cause of the cystitis should be sought for and if possible removed. Retention of urine, if it exists, should be relieved by the use of a catheter. When, however, the cause of the cystitis is one which requires an operation for its removal (calculus, stricture, etc.), it is usually best, unless in case of emergency, to defer interference until the acute stage of the disease is past.

If the inflammation is so severe as to involve surrounding parts and to give rise to pericystitis, the appearance of abscesses must be watched for with great care, as their early detection and evacuation is of cardinal importance.

Ordinarily an acute cystitis yields to careful treatment, and recovery is complete. If, however, the acute condition does not subside, or having subsided pyuria persists, the time has arrived for the more searching investigation referred to under Diagnosis.

Almost all cases of subacute or chronic cystitis, especially when associated with foul, decomposing urine, will be greatly benefited by thorough irrigation; and this measure may be employed in acute cases if the urine assumes a fetid character. When properly performed this washing out of the bladder usually does much good, but if done carelessly or improperly it may cause serious harm.

As a rule not more than two ounces of fluid shall be thrown into the bladder at one time. This rule is a good one in cases of acute cystitis, or when the bladder is greatly contracted or especially irritable. In many chronic cases, however, it is not only safe, but wise to distend the bladder somewhat with the injected fluid, the object being to spread out the folds of the mucous membrane so as to insure the thorough removal of fermenting mucus and the contact of the irrigating fluid with all parts of the bladder wall. If the injection is made slowly, the bladder ordinarily tolerates the distention well.

With regard to the injecting apparatus, a syringe forces the fluid in with irregular, intermittent force, and imperfections in the valves make it often a matter of uncertainty whether the proper amount has flowed into the bladder or not. These disadvantages are avoided by the use of a fountain syringe; and if a clear

glass bottle is used as the reservoir, it can be easily kept clean, and the exact amount of the fluid which flows into the bladder can be readily seen and exactly measured by a scale fastened upon the side of the bottle. The force of the stream is to be regulated by adjusting the height of the reservoir above the bladder. This should never be greater than from one to two feet, or the bladder may be subjected to a dangerous strain. It is also important to stop injecting the moment the patient feels the least desire to micturate.

The simplicity of this apparatus is of great advantage in point of cleanliness, and patients quickly learn to manage it for themselves.

The catheter used should be of soft rubber, if such can be introduced; if not, that form which passes with least irritation is the best, whether bulb-pointed or coudée, gum-elastic (English) or silver. A double-current catheter is less good than one with single caliber, for the continuous stream does not cleanse the bladder so quickly as is done by alternate filling and emptying, and the necessarily small size of the escape tube in a double instrument prevents the ready exit of thick pus or mucus. The bladder may also be irrigated without the use of a catheter by means of a fountain syringe with an olive-tipped nozzle. This is held tightly against the meatus and the fluid allowed to distend the urethra, which will "balloon" out as far as the triangular ligament. In this way the anterior urethra may be thoroughly washed, and then by raising the douche bottle higher, sufficient pressure may be obtained to overcome the resistance of the compressor muscle and the fluid will run back into the bladder. The whole operation is carried out without introducing any instrument beyond the meatus, and this method of irrigation has of late found considerable favor among surgeons in some parts of the country.

Many drugs are added to the injection fluid, either with the object of disinfecting the contents of the bladder or of acting topically upon the mucous membrane. The most useful solutions with which to irrigate the bladder are a solution of borax (biborate of sodium), a dram to the pint; boric acid two per cent., and chloride of sodium two drams to the pint. The stronger antiseptics, as corrosive sublimate and carbolic acid, are too irritating to be often useful. Occasionally when the secretion of pus and mucus is very abundant, and especially in chronic cases, permanganate of potassium 1 to 5,000 to 1 to 10,000 will be found useful for its astringent action.

In phosphaturia very dilute hydrochloric or nitric acid (one or two drops of strong acid to the fluid-ounce of water) may assist by their solvent and astringent action.

Lastly, we come to speak of nitrate of silver, which if properly used is productive of much good, but if abused or improperly employed may do decided harm. An obstinate chronic cystitis which does not yield to milder measures is sometimes greatly benefited by the use of a weak solution (one-tenth to one-fifth per cent.) of nitrate of silver. This gives the best results when it is used every second or third day, some milder injection being substituted on the intermediate days. The amount of pus is usually very decidedly diminished by these applications.

Occasionally, it happens that adhesive mucus so clogs the eye of the catheter as to prevent the escape of the urine. This may be removed by attaching a rubber tube full of water to the catheter and then dropping its free end into a vessel upon the floor. The weight of this column of water usually exerts sufficient suction to draw out the obstructing mucus.

In chronic cystitis, the local treatment is more to be relied upon than medication.

In the majority of cases the measures that have been suggested will accomplish, if not a cure, at least a palliation of symptoms which brings comparative comfort to the patient; occasionally, however, a case is met with in which the bladder has suffered such decided organic changes that the passage of urine through it, with its alternations of expansion and contraction, is sufficient to keep up an aggravated inflammation. In spite of every care the patient begins to suffer from septic absorption, and death seems imminent.

Under such circumstances, constant drainage by means of a catheter should be tried. This will often have the effect of giving the bladder the desired rest and allowing the reparative process to begin. If this is not successful, cystotomy holds out a last hope. It is now generally believed that the suprapubic route is the most efficient for drainage of this kind since it allows a more thorough investigation of the condition of the bladder and is more readily carried out under local anesthesia. In general, it may be said that it is rarely wise to give a general anesthetic for this purpose and that local or spinal anesthesia is to be preferred. The details of these procedures will be further discussed in the article, *Prostate, Diseases of the.*

Stone in the Bladder.—The stones which are commonly found in the bladder may be roughly divided into uric acid, oxalate of lime, and phosphatic calculi. A stone composed wholly of any one of these constituents is, however, not common, the usual condition being a mixed form, in which a uric acid or oxalate of lime nucleus is covered by a phosphatic crust; sometimes a succession of layers may be formed by alternating deposits of different components. The phosphates are almost always combined with alkaline urates and carbonates. Other substances, such as cystin and xanthin, in rare instances form concretions in the bladder.

For purposes of surgical classification, calculi may be divided into those which form in an acid and those which form in an alkaline urine. The former class includes the uric acid and oxalate of lime stones, while the soft concretions, composed mainly of phosphates, belong to the latter.

"The researches of Rainey, Harting, Ord, Ebstein, and others, indicate that the formation of stone is not a simple process of deposition of salts existing in excess in the urine. Indeed, instances are of every-day occurrence in which uric acid, the urates, oxalate of lime, or the phosphates are present in solid form for long periods of time in the urine without leading to stone formation. The investigations of these observers have shown the crystalline substances of the urine to follow the law of 'molecular coalescence' laid down by Rainey and elaborated by later observers; which is briefly, that 'in the presence of colloid or albuminoid substances crystalline materials become spheroidal in shape and coalesce in rounded form.' Following this law, in the urinary passages crystals of uric acid in their usual rhomboidal shape may for long periods be thrown down, washed along, and passed out with the urine without showing any tendency to form concretions. Finally, the irritation of the urinary tract leads to the exudation of albuminoid material, which, acting on the crystals, changes their molecular form and creates in them the tendency to coalesce. The necessary albuminoid material may be supplied in other ways. Necrotic bits of tissue are, as is well known, likely to be encrusted with lime salts. Masses of bacteria and bits of blood clot are also found in stones, but what part they play in the formation of the stone is not clear. The concretion, once started, continues to act as an irritant to the wall, and so continues to be supplied with an albuminoid envelope, in which successive layers of spheroidal crystals are deposited." (From A. T. Cabot's article in Morrow's "System of Genito-Urinary Diseases, Syphilology, and Dermatology," vol. i.)

The formation of phosphatic stones is almost invariably the result of inflammatory conditions in the urinary tract leading to alkaline fermentation of the urine.

Calculi may form in any part of the urinary apparatus. When they originate in the kidney they may find their way, sooner or later, into the bladder. This may be accomplished painlessly, or may be accompanied by severe pain (nephritic colic).

After reaching the bladder they either pass out through the urethra and cause no further trouble, or they remain and gradually increase in size until their presence is revealed by the symptoms to which they give rise. Their detention in the bladder is rendered extremely probable when some obstruction to micturition has caused dilatation with residual urine, or when sacculation of the bladder exists. A stone thus retained in the bladder continually grows by accretion. So long as the urine remains unchanged, the character of the stone continues the same; when, however, the urine, formerly acid, becomes alkaline from the occurrence of fermentation, the soft salts (phosphates, etc.) are deposited on the hard basis of calcic oxalate or uric acid.

Stones usually occur singly, but sometimes many, up to several hundreds, are found in one bladder.

Single calculi are moulded into a more or less oval form by attrition of the vesical walls. The surface may be tolerably smooth, as is often the case with uric acid calculi, or rough and granulated, as is more commonly seen in phosphatic stones; and finally, those composed of oxalate of lime are usually covered with rough, often sharp projections, giving them a knobby, irregular outline, which has suggested their distinctive name of mulberry calculi. When many calculi exist together in the bladder, they are usually smoothed and faceted by mutual attrition.

Stones vary greatly in size and consistency. Very large concretions were much more common formerly than now, when they come earlier to operation.

Phosphatic stones are usually soft and friable, though they may sometimes have considerable hardness. Uric acid makes firmer calculi, which are, however, tolerably brittle. The hardest stones are those made of oxalate of lime, and they may occasionally resist any but the most powerful lithotrites.

Stone in the bladder is often hereditary. A gouty or rheumatic diathesis, by favoring the production of acid urine, fosters the tendency to stone.

The habitual use of liquids or articles of food that easily ferment and give rise to acidity may increase the chances of stone formation. That the quality of the drinking water (presence of lime salts) has any influence, is not proved.

The geographical distribution of stone seems to be independent of any climatic or geological influences.

Dr. Keyes believes that the prevalence of stone in certain localities is to be in great measure accounted for by the hereditary nature of calculous disease, fostered by more or less close intermarriage.

Thompson states that stone is common in the children of the poor, but rare among old persons; whereas among the rich this state of things is reversed and the children are exempt, while their elders are oftener afflicted.

Symptoms.—The symptoms of stone in the bladder are: First, *pain*. This is especially severe at the end of micturition, when the bladder wall closes down upon the rough surface of the calculus. The pain is referred either to the end of the penis, or to the perineum and rectum. It is usually much increased by violent movements or jolting, as in riding. Secondly, *frequency of micturition*, which may or may not be diminished by rest in bed. Thirdly, *hematuria*. The presence of blood in the urine is intermittent. The water may be of a wine-red or smoky color, or the blood may be contained in the last few drops of urine passed. Hemorrhage is likely to appear after exercise or jolting. When these important symptoms are present, inquiry will often discover a history of previous attacks of renal colic, or of the appearance of gravel in the urine.

As confirmatory symptoms may be mentioned, sudden stoppage of the stream in the midst of micturition, caused by the stone falling against the urethral opening, and in children an elongated prepuce, owing to constant pulling in the effort to relieve pain felt at the head of the penis.

Diagnosis.—Until recent times the diagnosis of stone in the bladder has depended usually upon the possibility of touching the stone with a metal instrument. In the case of large stones, or those readily accessible from the neck of the bladder this was a very certain method but there are many pathological conditions frequently associated with stone which make it a very unreliable method, though one still to be employed in the absence of a better. In the adult male, stone formation is by far more common in connection with senile changes in the prostate which lead to residual urine. Under these conditions a stone may easily be missed by a searcher and in fact it may be impossible to touch it on account of mechanical conditions. All the uncertainty arising in this way, together with the doubt always felt as to the size and position of a stone, have been eliminated by the advent of the cystoscope. It could properly be said to-day that the cystoscope is the only thoroughly certain and always satisfactory method. It is applicable to all cases in which any instrument can be passed through the urethra and supplies us not only with all the evidence in regard to the size and position of the stone but also as to the other conditions in the bladder. A cystoscopy by a competent observer not only establishes the presence or absence of stone but enables the surgeon to decide what operation should be selected for relief of the symptoms. It would be difficult to lay too much stress upon the importance of employing the cystoscope in the diagnosis of vesical calculi whenever possible. In case the urethra is impassable to instruments by reason of stricture or the conformation of an abnormal prostate, stone can be detected with certainty by means of the *x*-ray in competent hands. This method, however, is far less satisfactory than cystoscopy as it gives no evidence other than the presence or absence of stone.

Prophylaxis.—Soft phosphatic stones are, as has been said, dependent usually upon a local condition of inflammation of the bladder, and any treatment, by irrigation or otherwise, which reduces this inflammation lessens the chances of stone formation. Uric acid and oxalate of lime stones, on the other hand, are of constitutional origin, and indicate faults of assimilation and tissue change which are in a degree amenable to constitutional treatment.

When a tendency to uric acid formation is evinced by the appearance of crystals in the urine, or by any symptoms indicating a gouty diathesis, efforts should be made to counteract this tendency by strict attention to the patient's habits with regard to food and exercise. Sugar in every form is harmful in these cases, as are also all fatty articles of food, and these should accordingly be avoided. Overindulgence in stimulating, highly seasoned dishes should be interdicted. Wine should be given up, and if the stimulant effect is needed, spirits, largely diluted, should be preferred. Systematic exercise should be taken—if possible, sufficiently violent to excite moderate perspiration, and the skin should be cared for by regular bathing and vigorous rubbing. If the patient be constipated, his bowels should be regulated, and this may well be done by a morning glass of Friedrichshall or Carlsbad water. Thompson recommends a long course of saline waters for these patients with uric acid tendencies, and regards their effect as due to a stimulant action on the liver. Whatever the

rationale of their use, they are of undoubted benefit when a constipated habit exists.

Lastly, general tonics, such as strychnine and quinine, may be of great service when the general health is debilitated. Alkaline diuretics, by correcting the overacidity of the urine, relieve local symptoms; but without the addition of general treatment the acidity returns quickly upon their disuse.

Treatment.—After the formation of a stone too large to pass through the urethra, its removal can be accomplished only by some mechanical expedient. The solvent action of alkaline or other remedies has never been shown to destroy a stone that had been proved to exist.

The choice of the operation appropriate to each case is to be decided both by the character of the stone and by the condition of the urinary organs.

Children stand the operation of litholapaxy very well. Occasionally the small size of the urethra makes this operation impossible, but, except in these cases, it is to be preferred to lithotomy.

The crushing of stone—lithotrity—became a recognized operation in 1824 through the efforts of Civiale, who, although operating with inferior instruments, obtained successes which demonstrated the possibility of pulverizing stones with instruments introduced through the urethra.

After that time the operation was greatly improved in technique, and largely displaced the earlier operation of lithotomy. (For the history of its development, see under the head of *Lithotrity*.)

In 1879 Prof. Henry J. Bigelow published a paper introducing the operation of litholapaxy (lithotrity at one sitting, rapid lithotrity), and so quickly did this procedure gain in favor that within a year or two of the publication of his first article it was a generally established practice; and the old operation of lithotrity, without complete evacuation, had become a thing of the past.

Professor Bigelow showed that the tolerance of the bladder to instrumentation is much greater than had been supposed, and demonstrated the fact that there is less danger in an operation, even long and tedious, which results in the complete evacuation of a stone, than in the usual short and repeated sittings for its more gradual removal. In short, he proved that the greatest danger of lithotrity is not from the use of instruments, but from the subsequent irritation of the mucous membrane by the fragments left in the bladder. To facilitate the rapid crushing and removal of stones, he also introduced improved instruments, which will be described under the head of *Litholapaxy*.

With these instruments it is now possible to dispose of many stones that would formerly have been thought beyond the reach of lithotrity, and it suffices to say that litholapaxy should be employed in all stone patients, except in cases falling under the following exceptions:

1. A very large and hard stone may resist every attempt at crushing.

2. A stone may have as a nucleus a foreign body, such as a piece of necrosed bone or a bullet, too hard to crush and too large to come through a tube.

3. An encysted stone may be out of reach of the lithotrite.

4. Some writers consider that stricture of the urethra may prohibit litholapaxy. This cannot often happen, for strictures, however close, yield readily to divulsion which may be immediately followed by the crushing and evacuation of the stone. We have so often seen these two operations successfully done together upon an etherized patient that we cannot but think this the best practice. While it economizes time, it saves the patient much needless manipulation. When an impassable stricture exists, perineal section followed by perineal lithotrity must be done.

5. The small size of the urethra in children may prevent the passage of instruments.

6. Hypertrophy of the prostate may occasionally render the passage of the lithotrite impossible and render lithotomy necessary.

7. False passages may exist, which so interfere with the introduction of instruments that the dangers of the operation are greatly enhanced, and the question of lithotomy is to be entertained.

8. The hip may be ankylosed in a position which interferes with the use of instruments.

Briefly stated, litholapaxy is the operation of election for all cases of stone in the bladder which do not require supracystotomy for some other purpose, such as hypertrophy of the prostate, or tumor.

HUGH CABOT

Bladder-wrack.—*Sea-wrack. Kelp-ware. Black-tang.* The plant *Fucus vesiculosus* L. (fam. *Fucaceæ*). This peculiar coarse sea-weed grows in the greatest abundance on the rocky Atlantic shores of both this country and Europe. At low tide it covers the rocks thickly with its prostrate greenish-yellow fronds, while, when the tide is full and the plant is enabled to float by the aid of its numerous air vesicles or "bladders," it covers the bottom with a forest of weeds. This is one of the plants which have been most extensively employed in the manufacture of kelp. It has also been considerably used in medicine as a deobstruent and alterative. Neither its composition nor its properties have been made well known, and its value is problematical. It contains one-fifth per cent. or more of iodine, in combination with potash. Rarely, considerable quantities of tannin have been observed in it. It has been loudly proclaimed as an agent to reduce obesity, and proprietary articles sold for this purpose are said to contain it. The dose is two to fifteen grams (ʒ ss. to iv.). Most manufacturing houses prepare both fluid and soild extracts. The dose of the latter is 0.3 to 2 grams (gr. v. to xxx.).

H. H. RUSBY.

Bladon Springs.—Choctaw County, Alabama.

POST-OFFICE.—Bladon Springs. Hotel and cottages.

ONE UNITED STATES GALLON CONTAINS:

Solids.	Vichy Spring. Grains.	Branch Spring. Grains.	Sulphur Spring. Grains.	Old Spring. Grains.
Sodium carbonate	46.33	41.21	34.93	32.89
Magnesium carbonate.	.29	.61	.65	1.36
Calcium carbonate.	.87	2.14	2.42	2.75
Iron carbonate...	.49	.23	.76	.02
Calcium sulphate.	2.25	2.79	2.96	.
Iron .	. . .	. . . .	. . .	.24
Sodium chloride..	. . .	.	. . .	7.69
Strontium.....	. . .	. .	. . .	.32
Silica. . .	.	.	.	2.10
Organic matter....	2.26	1.90	1.25	
Crenic acid..	. .	.		.75
Hypocrenic acid .	. .			.60
Total. . .	52.49	48.88	42.97	48.72
Gases.	Cubic inch.	Cubic inch.	Cubic inch.	Cubic inch.
Carbonic acid....	65.44	59.20	52.88	32.56
Sulphureted hydrogen...	.	.	.56	
Chlorine.....	1.84	1.84	1.84	
Total.....	67.28	61.04	55.28	32.56

Access.—The shortest route is by the Tombigbee Valley Railroad to Cullom Station, whence a drive of one and one-half hours to the hotel. Another route is by steamer from Mobile on the Tombigbee River, twelve hours. Daily communication during winter season. The springs are four miles from the steamer landing on the Tombigbee River. A railroad is being built within seven miles of the place.

For upward of thirty years the Bladon Springs have been a favorite resort for the best people of Alabama and the neighboring Gulf States. Before the Civil War Bladon was called the Saratoga of the South. The hotel is open all the year.

The location is about eighty miles from the Gulf as the crow flies, and about 170 feet above tide water. The climate is mild and equable, the mean annual temperature being 75° F. The nights are delightfully cool, averaging about 65° F. after eight o'clock during July and August. The surrounding country is hilly and heavily wooded with pines, and excellently adapted for thorough drainage. The resort offers abundant inducement for those wishing to escape the rigors of a Northern winter. Game is abundant during the fall and winter months, and it is said that deer are killed within a mile of the hotel.

The waters are of the alkaline type, quite plentifully charged with carbonic acid. They are useful in chronic indigestion, in syphilitic cachexia, in diseases of liver and spleen, in diseases of women, in advanced nephritis, in diabetes mellitus, and in rheumatism.

Emma E. Walker.

Blastoderm.—(Greek, βλαστός, a sprout, and δέρμα, skin.) The word blastoderm is used to designate the layers of cells which result from the cleavage, as distinguished from the unsegmented yolk of the meroblastic eggs.

The blastoderm merely represents one phase of a general process that occurs in the development of all Metazoa between the completion of the segmentation of the ovum and the formation of the gastrula stage. (See articles *Segmentation of the Ovum*, *Gastrula*, and *Area Embryonalis*.)

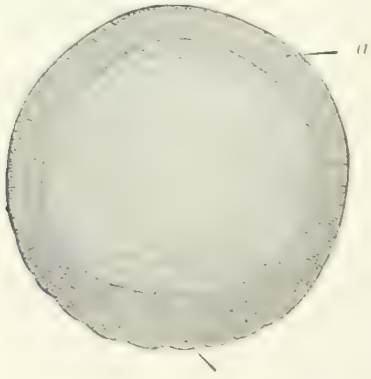

Fig. 654.—Blastula of Amphioxus in Optical Section. × 280. *a*, Micromeres of animal pole; *v*, vegetative pole. (After Hatschek.)

The process of cell-division that begins with the first division of the egg into two blastomeres in reality continues, not only until a late period of embryonic life, but also in parts of some animals throughout the life of the individual. But for the purposes of description, it is desirable to divide the embryonic life into stages, and the stage of the segmentation of the ovum is regarded as closed when the blastomeres lose their rounded outlines and form distinct epithelial layers of cells.

The stage following the segmentation, or cleavage, of the ovum is, in its simplest form, the *blastula*. This is a spherical or oval body consisting of a single layer of cells surrounding a cavity. The cavity is known as the *blastocœle* or segmentation cavity; and, following Hertwig, we may call the cellular envelope the primary germ-layer. The blastula is developed only from eggs that have a holoblastic cleavage. The typical blastula, in which the primary germ layer is only one cell deep, is met with in cœlenterates, echinoderms, and among the chordata in Amphioxus

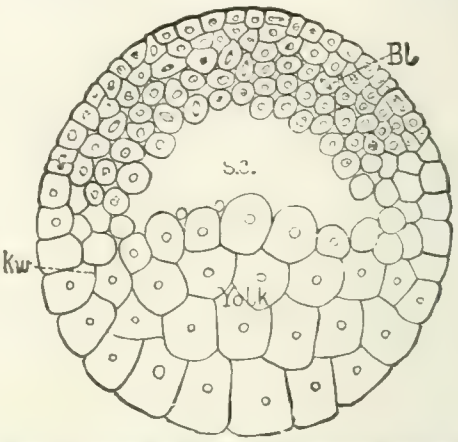

Fig. 655.—Blastula of Axolotl. Transverse section. *Bl*, Micromeres; *s.c.*, segmentation cavity; *Kw*, Kemwall germinal wall; *Yolk*, yolk cells. (After Bellonci.)

(Fig. 654). It rarely, if ever, happens that all of the cells of the blastula are the same size. Usually those at one pole are smaller than those at the other. The former is known as the animal pole; the latter, as the vegetative pole.

In Amphioxus the cells of the vegetative pole are somewhat larger and more abundantly supplied with yolk granules than the cells of the animal pole. This difference is emphasized in the blastulas of the lower vertebrates which have holoblastic eggs, the lampreys, the sturgeon, the Dipnoi and the typical Amphibia (Fig. 655). In these animals the primary germ-layer may be several cells deep and is always so at the vegetative pole; the lower hemisphere of the blastula being composed of a solid mass of large cells heavily laden with yolk granules. This mass merges gradually into the thinner layer of small cells that occupies the animal pole and covers the excentric blastocœle (Fig. 655). The subsequent history of the various parts of the blastula is discussed in the description of the next stage of development. (See *Gastrula*.)

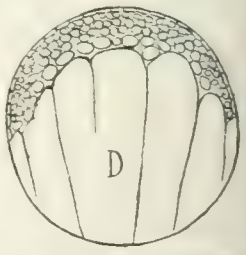

Fig. 656.—Vertical Section of a Late Stage of Cleavage of the Egg of Amia Calva. *D*, Yolk cells. (After Sobotta from Hertwig.)

The eggs of the fresh-water ganoids, Amia ("dog-fish" of the Great Lakes) and Lepidosteus (gar-pike) exhibit a condition that is transitional between meroblastic and holoblastic. The early cleavage planes extend slowly toward the vegetative pole and divide the lower part of the egg into several large irregular yolk-masses. These do not develop further, while segmentation proceeds rapidly at the animal pole, producing a cap of numerous small cells, the *blastoderm* (Fig. 656), which eventually grows around and encloses the yolk. Sections of an early stage show a small blastocœle under the blastoderm.

True meroblastic eggs are produced by the elasmobranch and teleost fishes, the Gymnophiona (blind snake-like burrowing Amphibia), Reptiles, Birds, and Monotremes. In these eggs the segmentation is confined to the animal pole and results in the

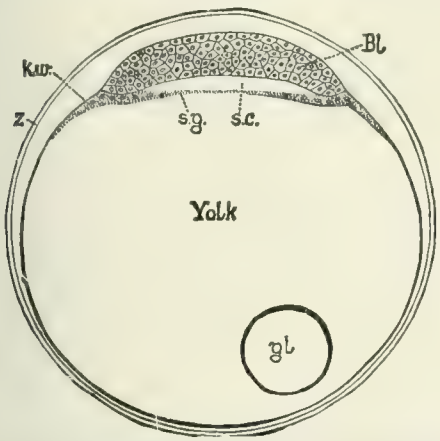

Fig. 657.—Egg of a Flounder in Transverse Vertical Section, Semidiagrammatic. *z*, Vitelline membrane; *kw*, periblast; *Bl*, blastoderm; *s.c.*, segmentation cavity; *s.g.*, subgerminal plate; *gl*, oil globule of yolk.

formation of a blastoderm composed of a layer of numerous small cells. This layer may be one or several cells thick. The yolk remains unsegmented for the most part, but it usually contains in the floor of the blastocœle (Fig. 657), especially near the margin, a number of periblastic nuclei, so that in reality the yolk is a syncytium, and the protoplasm surrounding the periblastic nuclei may become separated from the yolk, producing cells that are added to the blastoderm in the region of the germ-wall.

Fig. 658.—Egg of Scyllium Canicula. The lighter area is the blastoderm resting upon the darker yolk. The medullary groove is forming at the edge of the blastoderm. (After Hertwig.)

The blastoderm that has been produced by the segmentation of the ovum has been called the primary blastoderm. When, during the process of gastrulation, the blastoderm has been differentiated into three germ-layers, it becomes the secondary blastoderm.

There are two chief types of blastoderm: the *piscine* of elasmobranchs and teleosts, and the *sauropsidan* of reptiles, birds, and monotremes. In the former, the embryonal area appears at the posterior margin of the blastoderm and is continuous with a fold that extends on both sides for some distance around the margin of the blastoderm (Fig. 658) and finally forms the lip of the blastopore. That part of the margin which is not occupied by the marginal fold forms a zone of overgrowth which advances over the yolk with the growth of the blastoderm until the yolk is finally enclosed.

In the sauropsidan blastoderm (Fig. 659) the marginal fold is transitory, disappearing at an early stage, after which the whole periphery of the blastoderm consists of a zone of overgrowth (Fig. 660), which advances over the yolk and finally enloses it. The embryo arises near the center of the blastoderm in connection with the primitive streak, which is described with the other structures of the blastoderm in another article. (See *Area Embryonalis.*)

The blastoderm of the Gymnophiona shows some very interesting features intermediate in structure between the two main types.

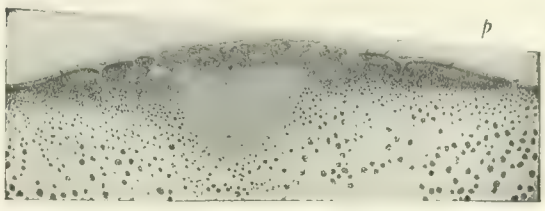

Fig. 659.—Transverse Section through the Center of the Blastoderm of a Pigeon's Egg taken Fourteen and One-half Hours after Fertilization. *p*, Periblast. (After Blount.)

In the mammals, there are three types of eggs corresponding to the three main divisions of the group.

The egg of the *monotremes* resembles a reptile's egg except in size. When the egg enters the oviduct it is 3.5 to 4 millimeters in diameter, which would be very small for a reptile of the same size as the mother, but much larger than other mammalian eggs. It is laden with both white and yellow yolk, consisting of discrete yolk-spheres and is surrounded by a vitelline membrane. In the oviduct it receives additional envelopes, a layer of albumen and a horny shell. While still covered by the shell the egg is laid and received into the mammary pouch where it hatches. While in the uterus, development proceeds, so that when the egg is laid the embryo of Ornithorhynchus

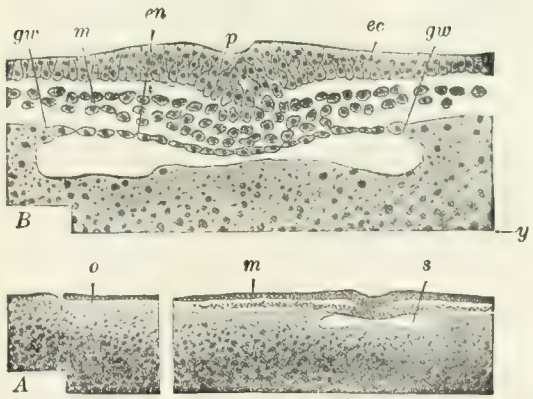

Fig. 660.—*A*, Transverse Section Through the Posterior Part of the Blastoderm of a Chick Incubated About Ten Hours. × 21. *B*, Median portion of the same. × 65. *ec*, Ectoderm; *en*, endoderm; *gw*, germ-wall; *m*, mesoderm; *o*, zone of overgrowth; *p*, primitive groove; *s*, subgerminal cavity; *y*, yolk. (After Duval.)

is in about the stage of a chick of thirty-six hours and the embryo of Echidna is about as far advanced as a chick at the end of the third day of incubation. (Wilson and Hill, 1907, p. 94.) But the most remarkable thing about the monotreme egg is that it grows, actually increases in both size and weight, while in the uterus after the formation of the shell, which appears to be added in the Fallopian tube. When it enters the uterus the monotreme egg including its membranes has a diameter of 4 to 5 millimeters; when laid its greatest diameter in Ornitho-

rhynchus is sixteen to nineteen millimeters and in Echidna somewhat less. (Hill, 1910, p. 93.)

In its earliest stages the blastoderm of the monotremes resembles the corresponding stage of a reptile or bird. Segmentation results in the formation of a discoidal blastoderm one or two cells thick lying upon a bed of white yolk (Fig. 661). But in the subsequent stages it shows two marked departures from the sauropsidan type. The first is the complete absence of any periblast or syncytial germ-wall; and the second is the very rapid extension of the blastoderm on all sides so as to entirely envelop the yolk, forming a complete single layered *blastocyst* in close contact with the vitelline membrane. As soon as the blastocyst is completed the egg begins to grow and the yolk is gradually converted into a fluid mass. At a stage when the liquefaction of the yolk has just commenced and the size of the egg has increased to 6×6.5 millimeters the blastocyst is found to consist of

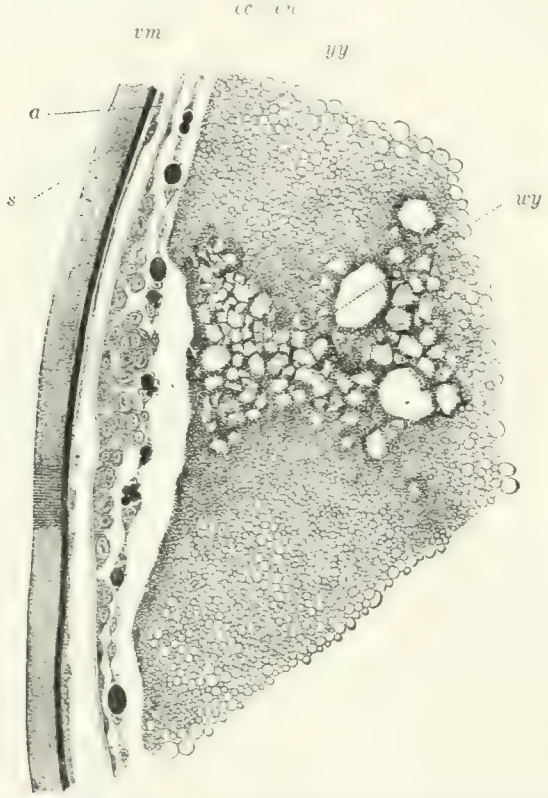

Fig. 661.—Vertical Section of Blastoderm and Yolk of Ornithorhynchus. × 245. *a*, Albumen; *ec*, ectoderm; *en*, endoderm; *s*, shell; *vm*, vitelline membrane; *wy*, white yolk; *yy*, yellow yolk. (After Wilson and Hill.)

two layers. The inner layer of "yolk-endoderm" consists of a single layer of cells, each cell being distended at the center by a vesicular nucleus and containing yolk spheres. The outer layer is for the most part composed of smaller very much flattened cells but in a small area 0.5 millimeter in diameter, probably at the animal pole of the egg, the cells of this ectodermal layer are larger and more closely packed, and are continuous with an underlying, loose, lenticular mass of rounded cells, beneath which is the one-celled layer of endoderm. This region is probably the beginning of the area embryonalis.

Our knowledge of the early stages in the development of the *marsupials* rests chiefly on the observations of Selenka on the opossum, Didelphys, and the observations of Hill (1910) on Dasyurus, the so-called "native cat" of Australia. The ripe ovum of Dasyurus consists of two substances. Toward one pole the ovum is composed of dense, slightly vacuolated, formative cytoplasm, which contains the polar spindle and occupies about two-thirds of the egg. The other third consists of deutoplasmic cytoplasm containing finely granular yolk material. The whole is surrounded by a distinct vitelline membrane, or zona pellucida. While very much smaller than monotreme eggs, the eggs of the marsupials are large for mammals, Dasyurus having an egg 0.24 millimeter in diameter, as against 0.07 millimeter in the mouse and 0.2 millimeter in man. After fertilization while passing down the tube, the egg of the marsupials receivestwo other coverings, a laminated layer of albumen and a thin shell membrane, which thickens in the uterus and apparently, like the shell of the monotremes, is capable of distention. Cleavage begins in the uterus and in the two-cell stage the deutoplasm of the ovum is seen to have been eliminated as a distinct yolk-mass which takes no further part in development, but becomes enclosed in the blastocyst and finally disintegrates. The first three cleavage planes are vertical, producing eight equal blastomeres arranged in a circle. The fourth plane is equatorial and unequal, dividing each blastomere into a smaller more transparent upper cell and a larger more opaque lower cell. From this interesting sixteen-cell stage a

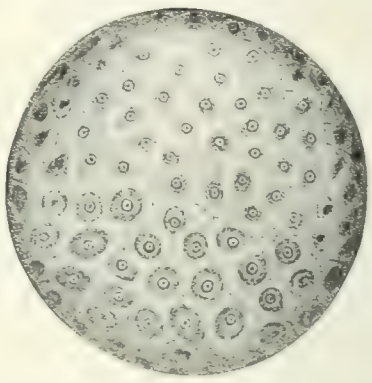

Fig. 662.—Blastocyst of Dasyurus, 0.6 mm. Diameter. Drawing from a photograph. × 80. (After Hill.)

single layered blastocyst is produced by subsequent cell divisions, all radial to the surface. The completed *blastocyst* (Fig. 662) is a sphere consisting of a single layer of flattened, polyhedral cells enclosing a tense fluid mass and pressing externally against the zona, which in turn is in close contact with the shell-membrane, the albumen having been absorbed. Study of the newly formed blastocyst (Fig. 662) shows it to be composed of two hemispheres, one of transparent cells derived from the upper ring of the sixteen-cell stage, and the other derived from the lower ring and rendered more opaque by a condensation of cytoplasm about the nuclei of the cells. During the growth of the blastocyst, this polar differentiation disappears, to reappear preparatory to the formation of the embryo. The upper hemisphere Hill believes to be the *formative* one in which the embryo is developed, and he infers that the other, the "tropho-ectoderm," is homologous with *trophoblast* of the higher mammals and gives rise to the external covering of the chorion. The establishment of the embryonal area is preceded by the appearance of an inner layer of cells in the formative hemisphere. This inner layer of "primitive endoderm" is produced according to Hill by cells which are differentiated in the outer layer and migrate inward. Confirmation of Hill's results is afforded by later ob-

servations made by Minot (1911) on the blastocyst of the opossum.

In the *Eutheria*, the ordinary mammals with which we are familiar, including man, the ova are very small (0.07 to 0.2 millimeter diameter), are very poor in yolk, and are never covered by any shell or shell-membrane. Rarely, as in the rabbit, the egg receives a coating of albumen during its passage through the Fallopian tube. The cleavage is holoblastic, but the result is very unlike the blastula of the lower vertebrates.

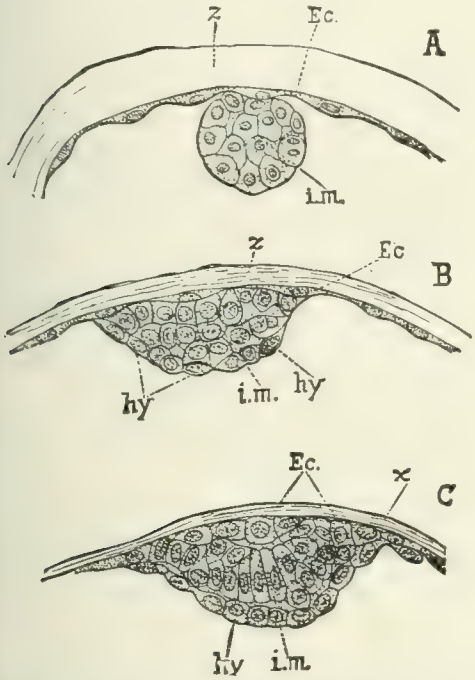

Fig. 663.—Sections Through Three Successive Stages of the Blastocyst of the Mole. *x* and *z*, Zona pellucida; *Ec*, trophoblast; *hy*, endoderm; *i.m.*, inner cell mass. (After Heape.)

In the marsupials, as stated above, the cleavage is radial and produces an open ring of blastomeres that give rise directly to a single layered blastocyst. In the Eutheria, on the other hand, the origin of the blastocyst is indirect. The first two cleavages produce a characteristic four-cell stage in which the blastomeres have a peculiar cross-shaped arrangement. At the close of the cleavage, the minute embryo is a solid mass of cells, or *morula*. In some cases the inner cells of the morula are found to stain differently from the outer ones, indicating a difference in constitution, and it has been suggested that the latter have grown around the former by a process of overgrowth, or epiboly. At any rate, the morula is soon converted into a blastocyst by the appearance of a cleft which separates the inner cell mass from the peripheral layer. The cleft rapidly enlarges by the imbibition of fluid from the uterus, the inner cell-mass remaining attached at one point to the inner side of the peripheral layer (Fig. 663).

This stage is characteristic of the Eutheria and has been found in all species in which the early ontogeny has been fully investigated. The inner cell-mass was called by Hubrecht the *embryonal knob* because it contains all of the formative material of the egg and from it are developed all the tissues of the embryo. The peripheral layer is strictly extraembryonic and to this layer Hubrecht has given the name *trophoblast*, because it is concerned with the implantation and nutrition of the embryo. It eventually forms the outer covering of the chorion.

According to Hill (1910), the embryonal knob is homologous with the formative hemisphere of the marsupial blastocyst, and the trophoblast, with the trophoectodermal hemisphere. The difference between the blastocyst of the marsupials and that of the Eutheria is due to the presence in the latter of a process or condition that Selenka (1900) has named *entypy of the germinal area*. He defines it as "the early enclosure of the formative cells in the interior of the egg," or "the separation of the germinal area in the interior of the blastodermic covering (chorion) during gastrulation and not by the formation of typical amnion folds." To bring this definition into harmony with present views, we must substitute "cleavage" for "gastrulation." The word "entypy" means a drawing or pushing inward, and is a convenient one to designate this peculiar condition of the eutherian blastocyst.

The subsequent history of the embryonal knob differs considerably in different species of mammals. Keibel (1910), following Hubrecht (1908) recognizes three main types of development. Type I is exemplified by the hedgehog and the bats. In these the trophoblast remains a covering over the whole of the blastocyst. In the hedgehog (Fig. 664) a space appears between the trophoblast and the embryonal knob which remains attached at its edges. The portion of the trophoblast thus separated is called by Hill (1910) the covering layer. After the embryonal knob becomes spread out to form the embryonal area; amniotic folds grow upward in contact with the trophoblast from the edges of the area, as described elsewhere (see *Amnion*), and enclose the space which then becomes the amniotic cavity. Hubrecht regards this as a very primitive condition. In the bats, the amniotic cavity is formed directly within the embryonic knob. Type II is found in the deer, sheep, and pig. In such forms, a cavity appears in the knob and extends to the exterior. It then opens, and with the expansion of the blastocyst the embryonal area flattens out, becoming a part of the general wall of the blostocyst without any covering layer. Type III

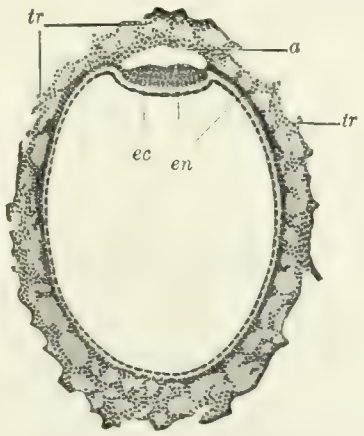

Fig. 664.—Section of the Blastocyst of a Hedgehog at the Stage when the Amniotic Cavity is a Cleft Between the Trophoblast and Formative Ectoderm. *a*, Amniotic cavity; *ec*, ectoderm; *en*, endoderm; *tr*, trophoblast. (After Hubrecht.)

is met with in the shrew, the dog, and the rabbit (Fig. 665). In this type no cavity is formed in the knob, which simply flattens out to form the embryonal area. Over this, the trophoblast persists for a time in the rabbit as a very thin covering layer. In the dog (Fig. 666) no covering layer is to be found at a very early stage.

Type I is of special interest because of the modifications of it that are found in the rodents and the Primates. In the mice, rats, and guinea-pig we have

the condition known as the *inversion of the germ-layers*. At one time this condition (Fig. 667) created a great deal of discussion, for what was apparently ectoderm was found to produce endodermal structures and *vice versa*. But it is recognized now that we have in these forms merely an exaggeration of the conditions seen in such animals as bats, with certain modifications. This condition is associated with a great development of the covering layer, which forms the first organ for the attachment of the embryo to the uterine wall, and has received the name ectoplacenta.

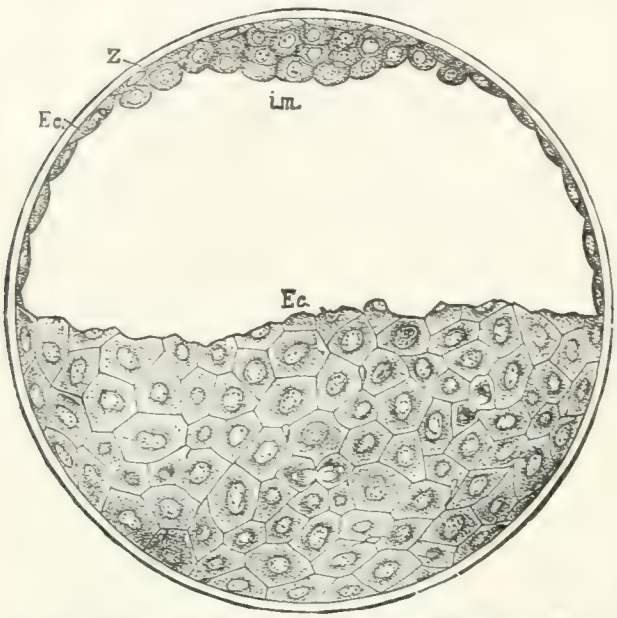

FIG. 665.—Blastocyst of Rabbit, Ninety-four Hours after Coitus. *Tr*, Trophoblast; *i.m.*, inner mass of cells; *Z*, zona pellucida. The upper half represents an optical section, the lower half a surface view.) (After Van Beneden.)

The blastocyst as a whole becomes cylindrical with the ectoplacenta (*Tr*, Fig. 667) at one end. This is greatly thickened and projects into the cavity of the blastocyst, pushing the embryonal knob before it, forming a central mass which nearly fills the cavity. The rest of the trophoblast, the parietal portion,

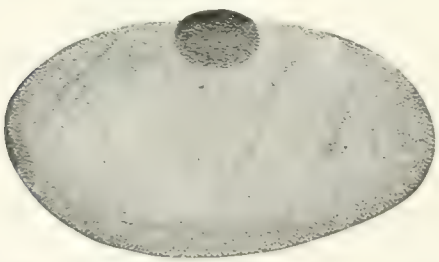

FIG. 666.—Surface View of the Blastocyst of a Dog, Eleven to Fourteen Days after Coitus. The darker portion is the area embryonalis. × 20. (After Bonnet.)

remains a single layer of cells, and in the mouse, according to Melissinos (1907), soon degenerates into a structureless membrane. The cells on the free surface of the embryonal knob become differentiated into a layer of endoderm (*En*, Fig. 667), that, like the finger of a glove, covers the central cylindrical mass and then grows over the inner surface of the parietal trophoblast, finally completely enclosing the cavity of the blastocyst, which then becomes the yolk-sac. In the deep part of the central mass is a sphere of formative ectodermal cells in which a cavity appears. A cavity also appears in the ectoplacenta and these two cavities may fuse to be separated again later by the development of amniotic folds. In the bottom of the two-layered pouch, consisting of formative ectoderm within (*Ec*, Fig. 667), and endoderm without, the area embryonalis develops. It is therefore strongly concave on its dorsal side.

In the Primates (the monkeys, apes, and man), the whole trophoblast becomes thickened, but the chief deviation from the ordinary blastocyst of Type I is in the development of the endoderm. This does not form a lining to the trophoblast but appears at a very early stage as a small vesicle, or yolk-sac, attached to the ectodermal vesicle and covered by a precocious development of mesoderm, which at first appears to fill the space between the embryonal knob and the trophoblast as a loose mesenchymatous tissue but later becomes concentrated into discrete layers covering the formative vesicles and lining the trophoblast (Fig. 668). The peripheral and the yolk-sac mesoderm are separated by a cavity, except where they are united in the connective stalk, or embryophore, (Selenka, 1900). There is, therefore, no union of yolk-sac and chorion. The early stages are imperfectly known, but the amniotic cavity appears to form directly as a space in the formative ectoderm, as in the bats.

An interesting summary of the fate of the trophoblast is given by Hubrecht (1908). In brief it is this part of the blastocyst that is chiefly concerned in what has been called the "implantation of the ovum" and, in connection with the allantois or its vessels, forms an important part of the fetal placenta. In the hedgehog, the anthropoid apes, and man there is a great proliferation of the trophoblast over the whole surface of the blastocyst (Figs. 664 and 668). In these cases, implantation consists in the complete enclosure of the young blastocyst within the mucous membrane on one side of the uterus. Under the action of the trophoblast the uterine mucous membrane is eroded to such an extent that the endothelium of the maternal capillaries is ruptured and the surface of the trophoblast is freely bathed in the maternal blood, this surface having greatly increased by the development of lacunæ or villi. Later a certain part of the trophoblast, the ectoplacenta, becomes differentiated into the fetal placenta by the proliferation of allantoic capillaries into the trophoblastic villi.

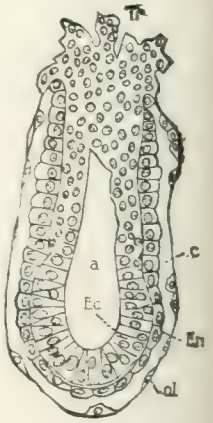

FIG. 667.—Early Embryo of Mus Sylvaticus. *En*, Endoderm; *c*, cavity of umbilical vesicle; *al*, trophoblast; *Tr*, proliferating trophoblast; *Ec*, embryonal ectoderm; *a*, ectodermal cavity, the lower portion of which is afterward cut off to form the amniotic cavity. (From Minot, after Selenka.)

In many mammals the proliferation of the trophoblast is confined to certain regions, the rest of it remaining a simple epithelial membrane. Reference has been made above to the very precocious development of the ectoplacenta in the guinea-pig and in the mouse (Fig. 667).

In some mammals such as the pig, the horse, and many lemurs, which present the extreme type of diffused placenta there is no proliferation whatever of the trophoblast. The uterine mucous membrane remains intact, but is provided with depressions which receive vascular projections from the chorion. There appears to be an interesting

inverse correlation between the size of the young blastocyst and the activity of the trophoblast. In the Primates and the rodents, with a very active trophoblast, the young blastocyst is very minute, while in the ungulates, with little or no proliferation of the trophoblast, the blastodermic vesicle acquires considerable size at a very early stage.

For further details the reader should consult Hubrecht's article referred to above, and also the article in Hertwig's Handbuch by Strahl (1902), whose views differ from Hubrecht's in many respects. (See also articles *Chorion* and *Placenta*.)

We have now traced in outline the variations of the blastoderm met with in the main groups of vertebrates from Amphibioxus to Man. We have seen almost a continuous series of forms from the simple blastula of the yolk-free egg of Amphioxus to the flattened blastoderm covering one pole of the richly endowed egg of the bird. Several series of parallel modifications could be cited from among groups of invertebrates, and these facts leave little doubt that in the course of evolution there has been a causal relation between the changes in the character of the blastoderm and the increased amount of food yolk in proportion to the protoplasm stored in the egg preparatory to development.

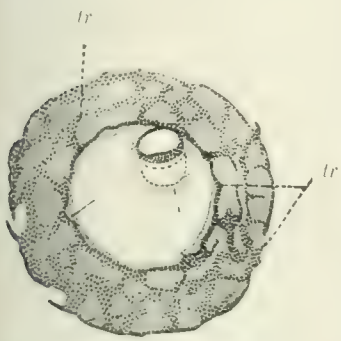

Fig. 668.—Diagrammatic Section of an Early Human Blastocyst. *tr*, Trophoblast. (After Hubrecht.)

In all vertebrates below the mammals, with a few rare exceptions, all the material that is to nourish the young, before it is able to take food by the mouth, is stored in the egg or else enclosed as an albuminous covering within the shell. But in the mammals a new method is adopted by which the embryo receives a continuous supply of nourishment directly from its mother. Even in the monotremes where there is a considerable supply of yolk this is by no means the chief source of supply for the developing embryo; in the marsupial egg there is very little yolk, and in the eutherians practically none at all. Associated with this condition we find in all mammals that the segmentation of the ovum results in the formation of a closed blastodermic vesicle, or blastocyst, and, as Hill has pointed out, this has furnished a mechanism for the absorption of material from the uterus. In the monotremes, whose eggs are provided with both yolk and shell, the development, except for the precocious enclosure of the yolk by the rapidly developed blastocyst, is essentially sauropsidian in character. In the marsupials, the yolk is so reduced as to have little influence on the course of ontogeny, but there is a firm shell-membrane which, serving as a mould, makes possible the development of the blastocyst as a single layered, hollow sphere. On the surface of this there appears an embryonal area closely resembling what is found in reptiles and birds. In the Eutheria a further modification is found in the entypy if the germinal area preceded by a morula stage. The condition which has brought about this change in the method of ontogeny Hill believes to be the complete loss of the egg shell and membranes, which leaves the egg without means of resisting the pressure of the maternal organs and makes necessary the very early arrangement of the embryonic cells in a closed vesicle that, by absorbing liquid, can expand and furnish room for the development of the embryonal area. Minot (1911) regards this explanation of the condition found in the Eutheria as the most satisfactory yet offered, and as probably correct. Although the loss of yolk in mammals results in the formation of a minute vesicular stage which superficially resembles the blastule of Amphioxus, it is essentially a very different structure, and in all mammals the area embryonalis and the stages immediately following closely resemble the corresponding stages in Sauropsida.

These considerations lead to the conclusion that the mammals have descended from ancestors that bore yolk-laden eggs, and comparative anatomy points strongly to the reptiles as the group containing the ancestral form, although there are some facts which point to an amphibian ancestry.

A very different conclusion is reached by Hubrecht (1908) who regards the holoblastic eggs of mammals as primitive and believes the trophoblast to be a larval envelope similar to what is found in certain invertebrates. He would regard both the mammals and Sauropsida as descended from a viviparous amphibian ancestor. The trophoblast has persisted in the mammals, according to his views, because it has become adapted to an intrauterine life, whereas in Sauropsida it has become vestigial because that group has secondarily acquired yolk laden eggs and the oviparous habit. These views of Hubrecht's, although brilliantly expounded and supported by a wealth of illustrations, are too revolutionary and too much at variance with the general conclusions derived from comparative anatomy to be acceptable to the majority of morphologists. Moreover Hill's demonstration (1910) that the Monotremes and Marsupials in their development show progressive transitional stages between the reptiles on the one hand and the eutherian mammals on the other, has still further strengthened the older and generally accepted views as to the relations of the vertebrates.

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Blastomycetes.—The Blastomycetes, or yeast fungi, are divided into two groups: (1) *Saccharomycetes* or true yeasts, in which true spore formation occurs; (2) *Torulæ*, in which no spore formation has been observed.

The Blastomycetes reproduce themselves by germination or budding, which distinguishes them from the Schizomycetes, or bacteria, which reproduce themselves by fission or division. From the Hyphomycetes or mould-fungi they are distinguished by being unicellular and by non-sexual reproduction. They are round or oval cells, usually many times larger than bacteria.

These organisms are of the greatest practical importance in various commercial industries, such as brewing, baking, etc., but as yet very little is known of their pathogenic properties in man. Certain varieties, when injected into animals, have proved to be tpahogenic and capable of producing tumors, and recently they have apparently been demonstrated (by Sanfelice, Plimmer, and others) in the epithelial cells in cases of cancer in the human subject; but what relation they bear, if any, to this affection is yet to be determined. They are not infrequently present in the air and in cultures made from the healthy throat.

Some varieties of Blastomycetes have been described which are pathogenic for mice, and in recent years (since 1894) there have been reported a number of cases of human infection from yeast. The pathogenic Blastomycetes may be briefly summarized as follows:

Saccharomyces busse, isolated in 1894 by O. Busse from the tibia of a thirty-one-year-old woman, who died thirteen months after the first symptom appeared. The autopsy showed numerous broken-down nodules in several of the bones, in the lungs, spleen, and kidneys. The yeast was cultivated from all these foci.

Saccharomyces transfaciens, isolated in 1895 by Curtis. The patient was a young man showing on the hips and neck multiple tumors having the gross appearance of softened myxosarcoma. This yeast is pathogenic for rats, mice, and dogs, only slightly so for rabbits and not at all for guinea-pigs.

Various similar cases have since been described, a number of them becoming generalized, and ending fatally. In general blastomycosis the lungs seem frequently to be the seat of primary infection.

The cases described first by Rixford and Gilchrist as coccidiosis due to *Coccidiodes immitis*—thought to be a protozoön—should be classed here, since Ophuls and, others have shown that the "Coccidium" formed showed the characteristics of yeasts. Dogs, rabbits, and guinea-pigs are susceptible to the fungus and show lesions similar to those in human beings.

A typical case of systemic blastomycosis has been reported by Fontaine, Hasse, and Mitchell (1909), with characteristic lung lesion. Lundsgaard reported a case of ophthalmia due to yeast. Pure culture obtained from the pus, showing the presence of yeast cells, in a severe hypopyon keratitis, inoculated into guinea-pigs produced abscess both at the site of inoculation and in the lymph glands. Buschke lisoated yeast from a cervical discharge, in which no gonococci were present, the blastomycete being pathogenic for guinea-pigs. Tokishige (1895) reported an epidemic among horses and cattle in Japan, known as "Japanese worm," "benign worm" or "pseudo-worm," which is caused by one of the saccharomyces. This is pathogenic also for rabbits, guinea-pigs and hogs. A similar disease, due to a species of yeast, has been identified in Italy and Southern France.

Recently Kartulis in Alexandria has described about a hundred cases of a skin affection occurring in the gluteal region of men and characterized by an elongated finger-like swelling, which breaks down and emits a purulent discharge forming an unhealed sinus. In the discharge and surrounding tissues are found numerous blastomycetes which have been shown to be a variety of the ordinary fermenting yeast (*Saccharomyces cerevisiæ*—Hansen). Kessler reported (1907) a skin lesion in an infant probably due to a similar blastomycete.

Judging from these reported cases, the yeast fungi may eventually prove to be of not inconsiderable pathogenic importance.

ARTHUR R. GUERARD.

Blastomycosis.—This comparatively recently known affection is of relatively very infrequent occurrence, though a number of cases have been observed and studied in this country, especially in Chicago and vicinity. It is known to be a specific affection, due to the pathogenicity of the yeast fungus, or saccharomyces; or at least to certain forms of the latter. Pathogenic activities of yeast fungi have been asserted at a much earlier date—for example, they

Fig. 669.—Blastomycetic Dermatitis. (Gilchrist and Stokes.)

were at one time accused of being the essential cause of tuberculosis and other constitutional maladies. But our modern knowledge of mycetogenic diseases, as far as the occurrence of granulomatous and internal lesions is involved, dates back to a period not very remote, in which it was shown, in connection with actinomycosis and mycetoma, that hyphomycetes (fungi in the technical sense) were able to cause an infectious group disease. The latter was naturally brought into relationship with the parasitic dermatoses due to other hyphomycetes, some of which, under certain circumstances, could also cause granulomatous lesions (so-called kerion).

Blastomycosis is clearly not a new disease, but one for many years overlooked; and was undoubtedly

confounded with localized tuberculosis—chiefly tuberculosis verrucosa cutis—with certain syphilides, and epitheliomata. Dermatologists have long known of manifestations which suggested one or the other of these affections at first sight, and even for prolonged periods; yet the course was eventually found to be benign, and the malady did not in any way respond to the treatment indicated in the known affections. Not all of these problematic affections could have been examples of blastomycosis; but the lesson was learned that supposedly incurable, destructive, and slowly progressive lesions of the skin could persist for years without involving the general health, and had absolutely nothing in common with lues or tuberculosis, save through a superficial or illusional resemblance.

FIG. 670.—A Microscopic Section of Blastomycetic Dermatitis, Showing Hypertrophied Epidermis (*e*) Numerous Miliary Abcesses (*a*) which Contain Parasitic Organisms (*p*). In the corium (*c*) are pseudotubercles (*n*) with giant cells (*G*) and parasites (*p*). (Gilchrist.)

The status of blastomycetic dermatitis was first established in 1894, when Gilchrist demonstrated before the American Dermatological Association sections, containing budding saccharomyces, from a lesion believed to have been a scrofulide. At very nearly the same period Buschke and Busse in Germany discovered, independently of Gilchrist, the same pathogenicity, not only in its local expression, but in its possibilities for general infection (one patient had suffered fatal pyemia from the saccharomyces). From this period onward the affection became recognized as both a local dermatitis and a generalized infection—the latter as compared with the former being extremely rare. The American dermatologists proposed the names blastomycetic dermatitis and blastomycosis; while the continental authors preferred the terms saccharomycosis, coccidiosis, etc. It may be remarked in passing that these discoveries gave an impetus to the doctrine of the hyphomycetic origin of cancer. Certain authors like Leopold of Germany and San Felice of Sicily were especially enthusiastic in this direction for many years.

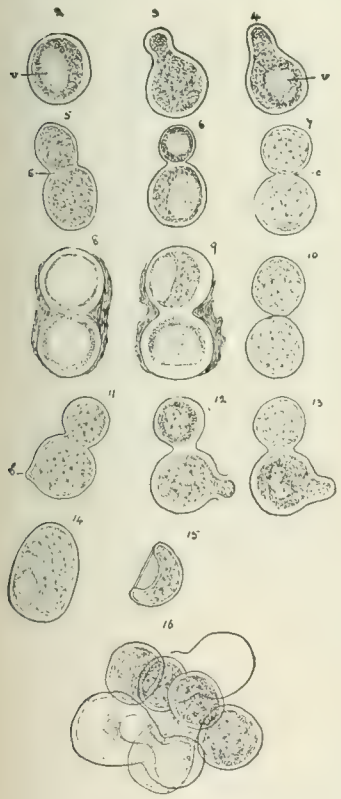

FIG. 671.—Some of the Individual Blastomycetes Found in the Section Shown in Fig. 670. Nos. 2–16 represent various budding forms; Nos. 8 and 9 show blastomycetes with some form of fibrous coating. (Gilchrist.)

SYMPTOMS.—The description of a beginning case does not necessarily apply to a long-standing instance. At some locality in the integument, presumably in one exposed to accidental inoculation, one or more indolent papulopustules appear, associated with an overgrowth of the papillary layer, with resulting appearance of a wart-like formation. The pus forces its way outward between the papillary prolongations which make up the wart and there dries to form a crust. One or a group of such papules may be in evidence, but the clinical expression is the same. Pus may not form at all; or it may appear only after squeezing. As already stated the pus does not proceed from a cavity or surface of any size but only from minute cavities—mere points to the naked eye. The pus forms entirely in the epidermis. The sensory nerve filaments are not involved, so that there is no pain or itching. New lesions may form close to the old ones or at some more remote points. The resulting patches may attain a variable size—usually not above that of a large coin, but exceptionally considerably larger.

It must be insisted further that the entire process is very superficial. The depth of infiltration does not usually reach half an inch, so that the increased thickness occurs only in the epidermis and overgrowth of the papillæ. When the dried pus and epidermis are removed we usually see papillæ which discharge pus and bleed freely. If the horny layer does not come away we see droplets of pus oozing from its interstices. Of ulceration in the ordinary sense nothing is seen as a rule until the disease has persisted for a time. But for some reason not understood ulceration often occurs in time with cicatrization; and as in other granulomata ulcers may heal spontaneously as they appear elsewhere. Circinate and serpiginous forms are not common, if they ever occur at all. One would naturally attribute this ulceration and scarring to secondary infection, but authors are silent upon this point. It is known that cicatrization is a notable factor in many cases. The scar may be smooth and supple, or deep and contractile, causing much disfigurement. Of special importance is the recrudescence of lesions in apparently well-healed ulcers. This phenomenon is of course common in other granulomata of the skin.

In regard to distribution, the lesions as already stated tend to appear on exposed parts, but they also develop repeatedly on the ordinarily covered tissues. There is no region absolutely immune—a fact which

compels us to believe that the affection may be and often is spread by autoinoculation. This fact is difficult of explanation, for we must bear in mind that itching is very unusual. The lower extremities, from the waist down, seem more exposed to attack than the trunk and limbs (with the exception of the hands). By far the greatest incidence is apparent on the face and hands. The favorite location on or near the eyelids, or in general on the upper half of the face suggests the similar preference of rodent ulcer. The prolonged isolated location about the eyes suggests a possibly primary focus for autoinoculation elsewhere. There is further a tendency to the production of ectropion in this locality. There is no typical enlargement or tenderness of the lymph nodes.

A word may be said as to constitutional involvement. This may or may not be consecutive to cutaneous lesions. But few instances are on record and these differ much among themselves. One subject after seven years of cutaneous blastomycosis developed symptoms of general infection which ended fatally. In certain cases of general outbreak the skin participated as if by secondary involvement. In a third series of cases there were no cutaneous lesions; the disease first attacked the vertebræ or some other deep-seated organ. It is evident that the internal or generalized cases are mostly autopsy material.

Fig. 672.—Photomicrograph from the First Case of Blastomycetic Dermatitis. (Gilchrist.) It shows one of the smaller miliary abscesses contained in the epidermis. Enclosed in the abscess are two blastomycetes, one of which belongs to the large budding variety (seen a little to the right of the centre of the field), whereas the other is a younger detached form which is seen directly below the former. These bodies are similar to those represented in Fig. 671.

Course.—Whatever the type of the disease the course is eminently chronic. In one instance we may see isolated lesions undergo apparent resolution with relapse in the scar. In others we have to deal with a perennial focus of disease which, while showing some

tendency to heal in spots, nevertheless continues to advance. The double tendency to heal and advance side by side may be expressed in many ways. A sudden spontaneous involution may be succeeded after a prolonged interval by recrudescence. Cases of indefinite persistence are known, and in any large community we may encounter dermatoses of which it may be said that they cannot be tuberculous, syphilitic, etc., for sufficient reasons, but that they have something in common with all.

Etiology and Nature.—Such a condition could not have been shown to exist before the modern developments of differential staining, cultivation, and inoculation. Gilchrist first revealed the nature of the malady by a study of the contents of one of the microscopic abscesses. Cultures of the fungus were obtained in pure state and inoculation tests showed that the affection could be produced at will in animals. Physicians have been accidentally inoculated, and as far as we know the disease is communicable only in this manner.

The fact that women are inoculated about as frequently as men is perplexing in a malady of this kind. The more the disease is studied the more it seems assured that age, race, sex, dwelling place, etc., are not of essential significance in its incidence. It may almost be affirmed that the secondary causes are quite unknown. In this connection may be mentioned the fact that the pathogenicity of the hyphomycetes which cause tinea, favus, etc., differs radically from that of the blastomycetes.

Pathology.—The process appears to begin as a proliferation of the rete cells, involving the production of minute abscesses. The derma may be involved secondarily with ulceration and scar formation. The horny layer may or may not be actively involved—in the latter case it may undergo proliferation with or without formation of epithelial pearls. The rete cells enlarge and swell, and leucocytes appear between them; the former also tend to dip into the corium, in the form of long epithelial processes such as are seen in certain epitheliomata. The simultaneous occurrence of overgrowth of epithelium and of abscess formation suggests an association of cancroid, plus a chronic infectious process. This symbiosis seems to be upheld throughout, and much depends therefore on the infectious factor, and its relationship to the frankly neoplastic element. A study of the former shows the presence of an active organism, which flourishes and proliferates chiefly in the minute abscesses often referred to, the contents of which are to some extent a culture of the said organism. When, however, we seek to fix the zoological status of the latter we at once encounter difficulties. From the strict bacteriological standpoint the case is by no means proven. Nonpathogenic cultures may be developed, and even among the pathogenic there is a wide range of activity.

The minute descriptions of authors concerning this or that species may be left out of consideration. It has long been known that in this field of bacteriology results are most inconstant. We can at the outset isolate various fungi for the different affections; it is only when we seek to cultivate permanently certain strains that we come to grief. We may of course contrast this dermatosis with other contemporary affections—such as the "protozoic dermatitis" of authors, an affection which comprises but a few recorded cases—the hyphomycetic dermatitis of Duhring and Hartzell, sporotrichosis, etc. But there is no longer any necessity for indirect routine methods of diagnosis, for the latter is easily accomplished as a rule.

Diagnosis.—This is made first of all by the characteristic clinical picture, which includes the minute abscesses, the contents of which should readily reveal the nature of the malady. A smear of pus from one of these abscesses, placed upon a slide, should first be treated with a few drops of thirty-three-per-cent. solution of potassic hydrate, and a cover-glass duly affixed. After an interval of an hour or less—sometimes within a quarter hour—the tissues and pus will have disappeared, while the budding organisms of the blastomycetes, resistant to the alkaline action, are still in evidence. In doubtful cases cultures may be made, and the Wassermann and tuberculin tests used

Prognosis.—There is no reason for death in a case of blastomycetic dermatitis; despite all the unfavorable features which develop in a chronic case, there is nothing to cloud the prognosis for ultimate recovery, or at least for arrest of the malady. On the other hand we know of internal blastomycosis only from autopsy records, and may conclude provisionally that this form is essentially fatal.

Treatment.—In the earliest days of our knowledge of blastomycosis it was assumed that a most vigorous local treatment was the sole indication. The curette and if necessary excision were the rational measures to be employed. With the increase of our general information, it was thought possible that iodide of potassium, because of its power over actinomycosis, was indicated in blastomycosis. This was tested with good outlook, but *x*-ray therapy was thought to be still more valuable, and at present both measures are jointly employed.

Naturally a full rational management includes both local and general measures; and it is seldom that the twofold indication is so clearly apparent as in the affection under review. All local resources, including the *x*-rays, intended to destroy morbid tissues, should be associated with the use of potassic iodide and other internal remedies of possible value in granulomata.

Dermatitis coccidioides, once regarded as identical with blastomycetic dermatitis, is now looked upon as a separate affection. Edward Preble.

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Blastopore.—(From the Greek βλαστός, a sprout, and πόρος, a passage, a way through.) The word *blastopore* was invented by Sir Ray Lankester (1877), who defined it as "The orifice of invagination by means of which invaginate planulæ acquire their endoderm." Planula is the name given by the same author to the embryo when it consists of only the two primary germ-layers, ectoderm and endoderm, and by "invaginate planula" he meant what is now always called the gastrula.

According to Haeckel's Gastræa theory, the gastrula is a stage of ontogeny that represents an ancestral type in which all the Metazoa have their origin, and which, in modified forms, persists among the living polyps and jelly-fishes to-day.

This hypothetically primitive type is the *Gastræa*, its primitive digestive tract is the *archenteron*, and its primitive mouth we may call *archistome* (thus translating the German word, Urmund, as did Minot, 1892). The *gastrula* represents the Gastræa in the ontogeny of animals now living, its cavity is also called archenteron, and its blastopore represents the archistome wholly or in part. In some animals the blastopore becomes the definitive mouth, in others it persists as the anus. In most animals it closes completely, and the mouth and anus are secondary openings, one or the other appearing at the point where the blastopore has closed.

The hypothetical Gastræa would be, like the living cœlenterates, a radially symmetrical animal with the main axis of symmetry running from the mouth to the aboral pole. It has been suggested that, in the course of evolution from the radial to the bilateral form, a new axis of symmetry has developed at right angles to the axis of radial symmetry, and that the archistome has elongated parallel to the new axis. With the elongation of the archistome has come a change in structure and a differentiation of function. The groove at the anterior end becomes an incurrent channel, and the groove at the posterior end, an excurrent one. Then the lips of the middle part of the archistome fuse to form the neural region of the animal, while the anterior groove becomes the mouth and the posterior one the anus. While such a view of the evolution of the bilateralia is purely hypothetical, it has, nevertheless, analogies among living cœlenterates, and is not incompatible with certain facts of embryology. These views as to the origin and significance of the blastopore and the fact that many important structures develop in or near its lips, have caused the blastopore to be the center of much interest and the subject of prolonged discussions among embryologists.

A typical blastopore is not to be seen in the ontogeny of all animals. It is to be found only in those forms which pass through a well-defined gastrula-stage. The groups which exhibit a well-marked blastopore are: Cœlenterata, Annelida, Mollusca, Crustacea, Echinodermata, Brachiopoda, Enteropnesta, Tunicata, Amphioxus, lampreys, ganoid fishes, Dipnoi, and Amphibia. In eggs that are heavily laden with yolk, the gastrula-stage may be so modified as to be hardly recognizable, and there may be an entire absence of a true blastopore. In the higher vertebrates, the process of gastrulation is complicated by being divided into two phases, with the result that several homologues of the blastopore appear to arise separately in the same individual. Although the

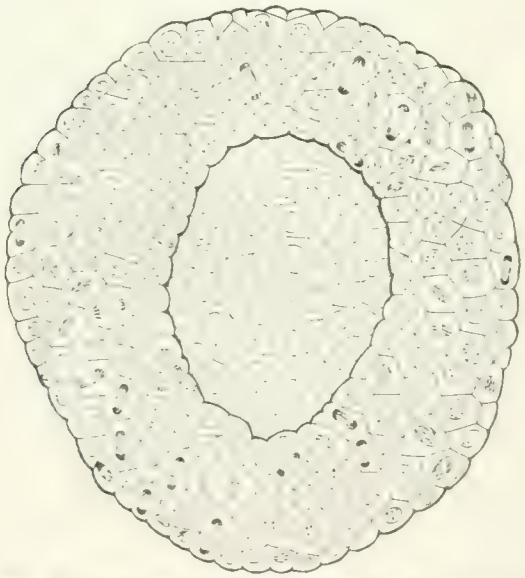

Fig. 673.—Gastrula of Amphioxus killed about 3 A.M., and mounted whole. The endodermal cells are visible through the blastopore in the center. Reduced from drawing made with Zeiss oc. 4, obj. 2 mm. (After Morgan and Hazen.)

eggs of placental mammals bear little or no yolk, the development of the embryo with respect to these structures is of sauropsidan type.

The blastopore being primarily the mouth of the gastrula, its origin and form are discussed in the article dealing with that stage of development (see *Gastrula*). The present article deals with the position of the blastopore relative to the axis of the egg, its position in relation to the axis of the body, its mode of closure, the derivatives of the blastopore in the vertebrates, and the structures derived in this group from the lips of the blastopore.

In regard to the position of the blastopore with respect to the primary axis of the egg, it may be said that, as a general rule, when a true blastopore is found it appears at the vegetative pole, or at any rate in the vegetative hemisphere of the egg. Hydra appears to be a remarkable exception to this rule.

In its relation to the orientation of the body, the primitive position of the blastopore appears to be at the posterior end of the long axis. It has this position

Fig. 674.—Sagittal Section of a Gastrula of Amphioxus at 4 A.M. *a*, Anterior pole; *d*, dorsal lip of the blastopore; *v*, ventral lip. Reduced from camera drawing made with Zeiss 4, oil immersion 2 mm. (After Morgan and Hazen.)

in the free-swimming planula larva of the Cœlenterates also in the larvæ of the echinoderms and of Balanoglossus. In the annelids, mollusca, and other groups with a spiral cleavage, the blastopore appears first as a wide opening at the posterior, vegetative pole and shifts later to the ventral side. In the chordata the blastopore seems to be formed on the dorsal side, and then to be shifted to the posterior end of the body.

The typical blastopore is a wide circular or elliptical opening (Fig. 673), by which the archenteron communicates with the exterior, and at its margin the ecto dermal and endodermal layers merge one into the other (Fig. 674). With the development of the embryo, this opening is reduced and in most cases completely closed. The method of closure may be concentric or excentric. It is concentric when the primary axis of the egg coincides with the principal axis of symmetry of the embryo. This occurs in the cœlenterates, in which group either the blastopore becomes the mouth or the mouth is subsequently formed where the blastopore closes. In most echinoderms, the blastopore becomes in a similar way converted into the anus, which subsequently shifts to the ventral side. In Balanoglossus the blastopore closes concentrically, and the anus later breaks through at the point of closure.

To demonstrate an excentric method of closure it is necessary to determine some point nearer one side

of the blastopore toward which the margins grow with unequal rapidity. This is not easy to do at a stage when the embryo presents few landmarks. Nevertheless, it is believed that the closure of the blastopore takes place in this manner in the majority of animals. In annelids, mollusca, and other groups with spiral cleavage, the closure is said to take place from behind forward, and in many annelids and mollusca the diminished blastopore becomes the mouth, or rather the inner opening of the stomodæum.

While many investigators have declared that in the vertebrates they could find no evidence for such a process, most students of vertebrate embryology regard the blastopore of the chordata as closing excentrically from before backward, and some claim with Cerfontaine (1906) that the blastopore as a whole changes position in the same direction.

In some vertebrates, as for example the spotted salamander, Amblystoma, the blastopore may be seen to close in such a way as to leave two openings leading outward from the archenteron. These are the *neurenteric canal* and the *anus*. In Amblystoma the blastopore, after being reduced to a small round opening, is closed by the approximation and fusion

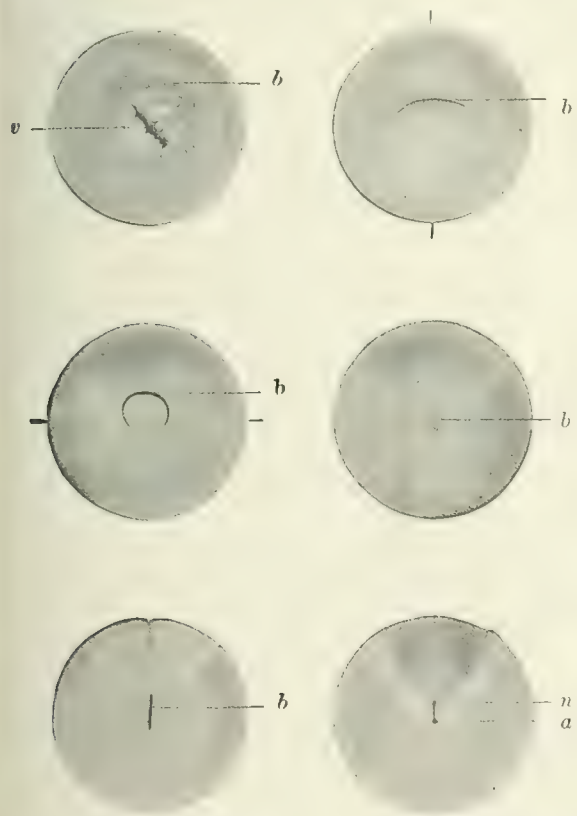

Fig. 675.—Surface views of successive stages in the closure of the blastopore of Amblystoma. × 12½. *a*, anus; *b*, blastopore; *n*, neurenteric canal; *v*, vegetative pole. (After Eycleshymer.)

of its lateral margins, Fig. 675. During this process it becomes a narrow longitudinal slit. The anterior angle of this slit persists for some time as the neurenteric canal, the posterior angle remains open as the permanent anus. When the anus appears as a new opening after the complete closure of the blastopore, as it does in most vertebrates, it develops in the same relative position as in Amblystoma and, therefore, may still be regarded as a blastoporic derivative. Likewise the neurenteric canal may develop apparently independently of any true blastopore, but, nevertheless, its anatomical relations are such as to cause it to be regarded as always a vestige of that more primitive opening.

In all amphibia the blastopore is infolded around a mass of endodermal cells, the yolk-plug (Fig. 676), which fills its orifice until just before closure and is then drawn inward. The ganoids exhibit transitions from this condition to that found in the eggs of the selachians, teleosts, and amniota where, associated with the presence of a relatively large amount of yolk, there is more or less suppression of the gastrula-stage, and a typical blastopore fails to appear. But, on the other hand, eggs with a large amount of yolk always present structures which may be regarded as homologous with the lips of the blastopore. These are the *marginal fold* of the blastoderm and the *primitive streak*. The distinguishing feature which these structures have in common with each other and with the lips of the bastopore, is the presence of a fold (the *ectental line*) where two germ-layers merge into one another. The marginal fold appears at the posterior edge of the blastoderm, which is homologous with the anterior or dorsal lip of the blastopore. In the fishes the marginal fold may extend rapidly on both sides until it involves the whole circumference of the blastoderm. In the sauropsida, on the contrary, it is never extensive and is soon surrounded by the zone of overgrowth and disappears. The primitive streak is especially characteristic of a little later stage in the development of sauropsida and mammals. That it is a vestige of the blastopore, is indicated by the perforation of its anterior end by the neurenteric canal and by the development of the anus or anal plate at its posterior end. (See *Area Embryonalis*.)

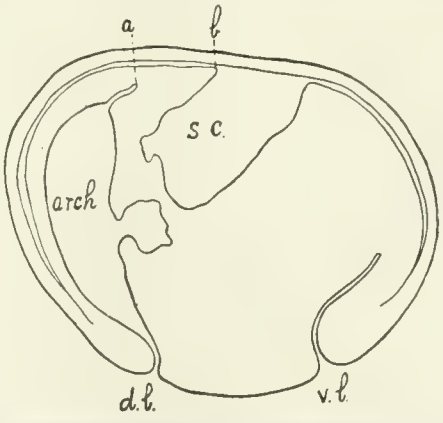

Fig. 676.—Sagittal Section of the Gastrula of a Tree-toad, Chorophilus. *Arch*, archenteron; *d.l* and *v.l*, dorsal and ventral lips of blastopore, the yolk-plug lies between them; *s.c*, segmentation cavity. Zeiss A, 2. (After H. V. Wilson.)

The relation of the blastopore to the body of the embryo, is a question that can hardly be regarded as settled, although it has provoked a discussion lasting forty years and has led to the production of voluminous literature. We may recognize three main theories as to this relation in the vertebrates: (1) The overgrowth theory, (2) the concrescence theory, and (3) the archistome theory.

According to the first of these, the closure of the blastopore is effected by the unequal growth of its lips toward a point placed excentrically near its posterior margin. The posterior, or ventral, margin is the place of least growth, the anterior, or dorsal, margin being the place of greatest growth. The axial structures of the embryo arise by the differentiation of the tissues in the dorsal lip of the blastopore, and elongation is produced by simple growth and differentiation backward.

Although it is not entirely original with him, the concrescence theory is to be chiefly attributed to the celebrated German embryologist, His, whose distinguished pupil, Minot, is its chief advocate in this country. The views of His were founded primarily on phenomena observed in the teleosts and selachians. According to this theory, the marginal fold of the blastoderm contains the rudiments of the two halves of the embryo. While the blastoderm grows over the yolk, these two halves are gradually brought together, beginning at the cephalic end (Fig. 677). Minot (1892) defines concrescence as the growing together of the two halves of the ectental line to form the structural axis of the future embryo.

The archistome theory (Urmundtheorie) founded by O. Hertwig, is very similar to the concrescence theory, but differs in the following particulars: (1) In emphasizing the character of the blastopore as a vestige of the archistome; (2) in distinguishing two parts of the margin of the blastoderm, the marginal fold representing marginal lips and the zone of overgrowth where the process of cleavage is not complete; and (3) in recognizing that the blastopore is not a structure having a fixed position, but that, beginning at the anterior end, it may migrate along the median

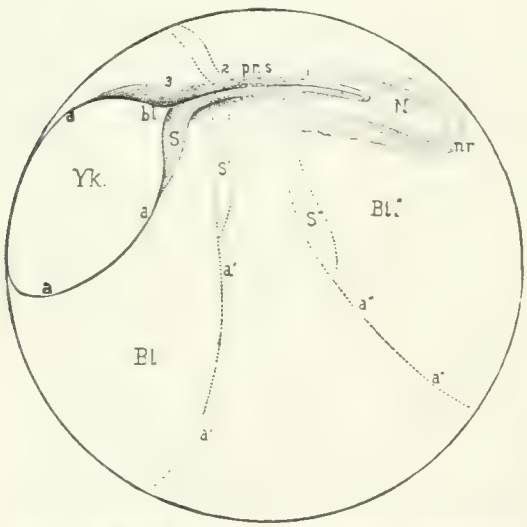

Fig. 677.—Diagram to illustrate the theory of Concrescence: *Bl*, blastoderm; *bl*, blastopore; *a''*, *a'*, *a*, successive stages in the closure of the blastopore; *N*, medullary groove; *nr*, neural ridge; *pr. s*, primitive streak; *s*, thickened edge of blastoderm; *Yk*, yolk. (From Minot.)

line the whole length of the archistomal region. According to this theory the anterior lip of the archistome gives rise to only the anterior part of the head of the embryo, and the rest of the axial structures are formed from the lateral margins of the archistome, which unite in the mid-line. The anus marks the posterior end of the archistome.

Hubrecht holds similar views as to the relation of the archistome and axial structures, but he lays especial stress upon the idea of gastrulation in two phases, and differs widely from Hertwig as to the origin of the mesoderm and in other details. To give a history of these theories with a summary of the evidence for and against each would require an amount of space that is prohibitive. Therefore for further information it is necessary to refer the reader to the works cited in this list which follows, and to related articles in this Handbook, viz., *Blastoderm, Gastrula, Germ-layers, Mesoderm, Neurenteric canal*, etc.

Robert Payne Bigelow.

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Blattidæ.—The name given to the cockroach family. Several species are common inhabitants of dwellings. Some are known to carry stages in the life cycles of certain parasitic protozoans, and it is believed by some writers that these insects may even harbor minoparasite pathoganic in man. See *Insects*.

Blaud, P.—Born in 1774 at Nimes, he was educated at Paris and began the practice of medicine there in 1805. Little is known of his life beyond the fact that he was a very successful practitioner and, in spite of the demands of a large clientele, was a prolific writer. Among the more important of his contributions to medical literature were: "Nouvelles recherches sur la laryngo-trachéite connue sous le nom de croup," 1825; "Traité élémentaire de physiologie philosophique ou élémens de la science de l'homme, ramenée à ses véritables principes," 1830. He also contributed many articles to various medical encyclopedias and to the medical journals, on "compression of the carotids for the relief of cerebral congestion," "influence of the muscular system on the circulation," "fibrinous concretions of the heart," "the chlorotic diseases," etc. In the last named essay he described the iron pill, which is known as Blaud's pill to this day, the originator being, however, usually regarded as a German, owing probably to the fact that the pill was strongly recommended by Niemeyer in his treatise on the Practice of Medicine. The formula of this pill is as follows: ferri sulph. pulv., potass. carb., āā ℥ss, gum tragacanth, *q.s.* to make ninety-six pills. Blaud died in May, 1858. T. L. S.

Blennostasine.—A compound derived from one of the cinchona alkaloids. It is said to be cinchonidine hydrobromide. It is hemostatic, astringent, and sedative to the central nervous system. It has been used in catarrhal inflammation of the respiratory mucous membrane, influenza, colds, hay fever, etc., in doses of gr. i. to iv. (0.06–0.25).

R. J. E. Scott.

Blepharospasm.—Von Michel restricts this term to the tonic spasm of the orbicularis, applying to clonic spasm the expressions blepharoclonus, spasmus

nictitans and nictitatis. In the article on blepharospasm in Wilbrand and Sänger's "Neurologie des Auges" the affection is described as a spasmodic state which may involve, beside the orbicularis muscle, the corrugator supercilii and frontal portion of the occipitofrontalis. Generalizations like the preceding appear to show that the teachings on this subject are in need of standardization, and this impression is borne out by further consideration. It appears to be impracticable to separate the tonic from the clonic form, for in many cases of the latter the contractions occur in a muscle already the seat of increased tonus, while tonic and clonic forms may occur in the same subject. Such cases are termed mixed. Indeed perfectly pure tonic blepharospasm is said to be of infrequent occurrence.

Tonic blepharospasm may occur either in accesses or as a persistent contraction which in its highest degree closes the palpebral fissure and thereby constitutes a form of blindness; for in the vast preponderance of cases all blepharospasm is bilateral. It is always difficult and sometimes impossible for the patient to force apart the closed lids. In thus endeavoring the patient contracts his corrugators and frontalis muscles, and throws the forehead into deep transverse folds. There may be further associated movements of other facial muscles. The patient may be compelled to open his eyelids with the fingers.

The greatest variation is seen in the intensity and duration of the spasm. The latter may be very transitory lasting but a few minutes, or may persist for weeks; and individual attacks may rapidly follow one another. In the latter case the muscle may not be wholly quiescent during the intervals but may show an increase of tonus. In serial attacks there is a notable absence of periodicity, while the duration and severity show no regularity. Sometimes we see particularly severe attacks follow long periods of quiescence. Accesses tend to appear without warning, so that the fear of becoming suddenly blind has an unfavorable effect on the psyche. Certain effects may both precipitate and cut short the attacks. Chief among these are influences which concentrate or divert the patient's attention. Sleep usually causes cessation of the spasms, but sometimes they set in during slumber. Hence, blepharospasm often has a psychogenous component independent of any actual material causation. Subjects may recover promptly or fail to recover at all by reason of this factor.

While there is an essential type of blepharospasm without associated movements of any kind, it is perhaps rather rare. As a rule there is more or less involvement of other muscles supplied by the facial nerve.

The clinical types of blepharospasm may be grouped in various ways. Michel divides them into involuntary, voluntary, and reflex. They may also be divided according to origin into central and peripheral. The involuntary form is chiefly an accompaniment of various neuroses or of organic disease of the central nervous system—in detail ti s, epilepsy, hysteria, traumatic psychoneurosis, chorea, tetanus, tetany, paramyoclonus, myotonia, and any organic disease involving the facial area of the cortex, the proper cerebral paths, and facial nuclei (such as tumors, hemorrhages, softening, abscesses, etc., etc.). The involuntary type may show great variation in intensity and duration and in the associated phenomena, which latter also vary necessarily with the cause.

Voluntary blepharospasm, so called, is simply a habit spasm which at first may be controlled by the will, but eventually becomes of the nature of an imperative concept. This type of affection may be accompanied by associated movements of the face and head. The spasms always cease during sleep. In certain cases this form of habit spasm becomes a confirmed part of the individual's make-up and is useful for identification. The subjects are said to "snap" or "bat" their eyes, and "snapper" or "blinky" becomes a familiar descriptive nickname. The affection which begins in childhood is, however, outgrown and is seldom seen after adolescence. The clinical expression is an incessant winking, and the term blepharoclonus is largely synonymous with it. But not all of these cases are examples of habit spasm. Some may represent the inception of a chorea, while others are doubtless reflex, in part at least, and due often to visual anomalies. Fibrillary twitching of the orbicularis, which is usually quite a different affection, may be encountered in all forms of blepharospasm, and may be an isolated symptom.

The involuntary and "voluntary" forms, however numerous and varied they may be, really make up but a small proportion of all the cases of blepharospasm. The great majority are reflex, and require a centripetal irritation to bring out the motor disorder. An element which enters strongly into the reflex is increased sensitiveness of the centers involved. Given this factor, the peripheral irritants which suffice are numerous and show much variety. The starting point may be anywhere in the region supplied by the trigeminus, although its first branch naturally is most frequently concerned.

In the great majority of cases the irritation proceeds from some inflammatory affection of the bulbus oculi, notably the cornea, iris, and ciliary body. The nature of the blepharospasm is in all such cases readily apparent. Despite the fact that in many cases but one eye is the seat of a lesion, the spasm is usually binocular. In all cases of this type we see a triad of symptoms—lacrymation, photophobia, and blepharospasm. The spasm tends to persist, to be constant, as long as the eyes are inflamed. It may increase and diminish in proportion as the lesions become aggravated or improve. After protracted closure of the eyes, exposure of the latter to the light may be attended by transitory blindness. Foreign bodies and various traumatisms set up blepharospasm, and any case of the disease of whatever nature which sets in in the elderly is prone to become confirmed.

The mere enumeration of the conditions which have caused blepharospasm through irritation in some portion of the trigeminus area would require much space. In this connection the so-called pressure points should be mentioned. Compression of a sensitive area, notably a sensory nerve trunk, is sometimes sufficient to cause blepharospasm; while in other cases it may arrest the latter. Among peripheral irritations which have to be considered in the treatment should be mentioned especially carious teeth.

Irritation of the retina is a potent cause of blepharospasm of a severe type. Bright lights or certain colors (red or blue) and the dazzling reflection from snow, ice, water, etc., may be mentioned in this connection.

A certain occupation neurosis or professional cramp incidentally entails a blepharospasm; this is the jeweler's tic, which results from habitual use of the monocle. The compression of the latter by the left orbicularis causes contractions of all the muscles supplied by the left facial nerve, most marked in the upper and middle divisions of the latter. The affection appears to be a pure motor neurosis, as if due to a quantitative increase in the innervation impulses of the facial.

Diagnosis.—Aside from the necessity at times of excluding ptosis, the question of diagnosis hardly becomes active in connection with so obvious an affection as blepharospasm. In the rare cases of the latter in which muscular contraction is not in evidence, even when it is attempted to force the eyelids apart, the spasms may be induced by stroking the lower lid,

or suddenly releasing the eyeball after first compressing it. Michel states that after transitory facial paralysis the orbicularis twitches as it resumes its activity.

Treatment.—This is based wholly upon estimation of the causal factors. Since a neuropathic substratum is very probably present in a majority of all cases, institutional treatment with especial reference to hydrotherapeutic and other physical measures may be demanded in protracted cases of any type. The psychogenous element may also make expedient a course of psychotherapeutics, with special emphasis upon suggestion and inhibition therapy. In order to determine the importance of the reflex element in these cases it is advocated in some quarters to make use of morphine hypodermics and even of general narcosis. These measures often prove curative, although not eligible for routine use. Another method of quickly impressing the reflex element is cocainization of the conjunctiva, with either a solution of the alkaloid or a ten-per-cent. cocaine-vaseline ointment. Plunging the face frequently in cold water is a simple method of achieving the same result advised by von Michel. The element of photophobia, in so far as it may be a cause and not a mere accompaniment of the spastic state, may be eliminated by wearing smoked glasses. The tendency of the patients to seek darkness by other means must be combated. All forms of corneal and iridocyclical inflammation must, of course, be treated *secundum artem*, and when no adequate cause for reflex irritation is apparent authors unite in recommending galvanism.

Various surgical procedures have been invoked to cut short severe blepharospasm by interrupting the reflex arc at some point. The latter may be in the course of the motor or sensory fibers concerned. These procedures range from section of the muscle (external canthotomy) to stretching or section of the facial nerve or parenchymatous alcohol injections. As these interventions cause motor pareses, albeit transitory, similar operations on the trigeminus apparently have the preference. When disease of the sensory nerve is actually the cause of the reflex blepharospasm the indication for operating upon it is very plain. In certain cases local measures are indicated, as in carious teeth, aural lesions, intranasal mischief, and other peripheral affections.

EDWARD PREBLE.

Blind, Education of, and Occupations Open to the.—The handicap of the blind—the loss of sight—renders their education and occupational training a peculiarly difficult problem. So many of the impressions which ordinarily go to make up our education are received through the visual function, that its absence necessitates very radical changes in the method employed. For many years the difficulties presented by this deficiency were regarded as insurmountable and the blind existed in a practically imbecile condition, mental development being largely inhibited. Later it was realized that the education of the blind so that they might read and write could be accomplished through the sense of touch. The acuity of impression which can be gained by this means is remarkable and there have been trained blind persons of the greatest culture and accomplishment.

This development has, however, been one of comparatively recent years. While there were some asylums for the blind founded prior to modern times, as one in Cappadocia in the fourth century and one in Syria in the fifth century, they were refuges only and contemplated no plan of constructive education. A government hospital was founded at Paris in 1260, this institution being in existence to-day. From this time on there is record of sporadic efforts to educate blind individuals but there seems to have been devised no methods of particular merit.

One of the first to conceive the idea of the touch system of reading and education was an Italian physician named Cardan (c. 1500) who had become interested in the physically handicapped through his work for the deaf. During the early part of the sixteenth century Lucas, a Spaniard, and Rampazetto, an Italian, used carved wooden letters for teaching the blind. In 1749 Denis Diderot, the French litterateur wrote an essay on the lot of the blind which attracted considerable attention and to which frequent reference has since been made. The education of the blind has been inseparably connected with the development of the touch system of reading. After efforts with movable types, the faces of which the blind could feel, the next advance was made by a blind German, Weissembourg, who in the instruction of Marie Thérèse von Paradis used letters cut from cardboard. Later she learned to read words pricked by a sharp point on the same material.

The use of characters embossed on paper, the medium which has since been used in books for the blind, was originated by Valentine Haüy, a Frenchman generally regarded as the father of education for the blind. Haüy was impressed with the misfortune of the blind after witnessing a burlesque of a musical entertainment by several blind men attired as buffoons. He resolved to do what he could to ameliorate the condition of the sightless and took as his first pupil a blind boy named Leseuer. This pupil while going over some printed material found a sheet bearing an exceptionally heavy type impression, several letters of which he was able to distinguish through the sense of touch. When this was brought to the attention of Haüy he impressed on paper some other characters which were read by the boy. This incident is said to be responsible for the inception of printing in relief.

The first books were made by embossing on paper letters practically identical with ordinary italic script. This system spread to England where an attempt to improve it was made by James Gall of Edinburgh. Other work was done about the same time by Alston of Glasgow, Howe of Boston, and Friedlander of Philadelphia. Gall made great claims for his system which involved the use of regular capital letters with curves eliminated and angles thrown to the outside substituted in their stead; his theory was that the outside contours of the letters were more distinguishable to the touch than the outlines of the inside. His plan, however, seems to have met with little favor though several schools for the blind gave it determined trials. In 1827 Gall did the first printing under his system and in 1834 issued the *Gospel of St. John* in his embossed text. The Society of Arts of Edinburgh in 1832 offered a prize for the best system of embossed printing for the blind. After considerable deliberation Gall's plan was rejected and the award made to Edmond Fry who submitted an alphabet which consisted of capital letters with the smaller strokes omitted. John Alston of Glasgow became the most prominent user of this new system, raising a fund of contributions and securing a government grant to aid the work. In 1838 he issued the New Testament in Fry's type and 1840 the complete Bible.

In the United States the first embossed printing for the blind was done in 1833 almost simultaneously by Samuel Gridley Howe in Boston and Friedlander in Philadelphia. The former used lower case letters exclusively, the curves being replaced by angles; the latter used plain capital letters only. Two stenographic systems of printing were advanced in England by Lucas and Frere. The next system which was devised has proven of great value. Its originator was William Moon, himself blind, who promulgated it in 1847. The Moon type as it has since been called, bears a general resemblance to regular capital letters. All unnecessary parts were omitted and some radical

changes were made to make the embossed letters easily distinguishable to the touch.

Up to this juncture all the systems proposed had been based on an adherence, more or less close, to existing characters in ink printing or writing. They are all known as line types. An epochal advance was made by the introduction of a point system—that is an alphabet formed by different combinations of embossed points. Charles Barbier, a French army officer devised a system of speech sounds represented by units embracing twelve positions in which varying numbers of raised dots could occur. The particular sound was determined by the number and location of the dots in the possible positions. Each unit was made up of two vertical rows of six points or positions each. The objection to this system was that the number of dots used was too great to be easily sensed by touch and thus read. But is was reserved for a blind man to create the first alphabet destined to come into general use.

A teacher in the Institution Nationale des Jeunes Aveugles, Louis Braille, in 1834 brought forth an alphabet similar in general principle to that of Barbier but with the number of point positions reduced to six. These positions are arranged in two vertical rows of three points each. This system is now known as European Braille. In the United States there sprang up later two other point systems known as American Braille and New York Point. In both these systems it is so arranged that the most frequently used letters have the simplest dot combinations.

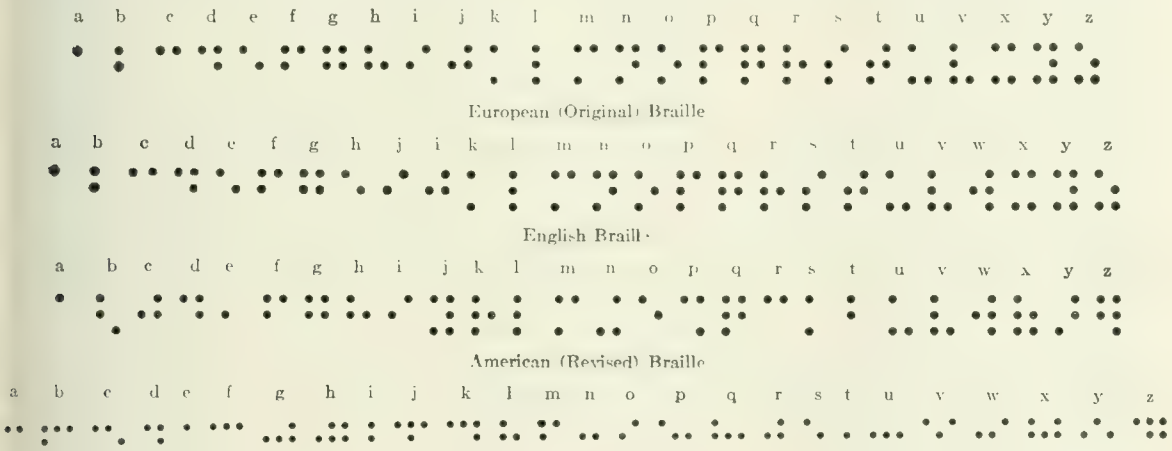

a b c d e f g h i j k l m n o p q r s t u v x y z
European (Original) Braille
a b c d e f g h j i k l m n o p q r s t u v w x y z
English Braille
a b c d e f g h i j k l m n o p q r s t u v w x y z
American (Revised) Braille
a b c d e f g h i j k l m n o p q r s t u v w x y z
New York Point

Fig. 678.—Blind Alphabets in the European and American Point Systems.

The four last mentioned systems of embossed printing are now in use. Apart from any consideration of the merits of each it is unfortunate that this should be the case. Were there a uniform type the development of literature for the blind would be an easier task. For example the *Matilda Ziegler Magazine*, a periodical furnished without charge to all blind persons in the United States, has to be issued in two editions using different types. The blind educated in some institutions read one type, those educated in others, read a different one.

The original braille type generally known as "European Braille" is in use on the Continent, in Great Britain, Egypt, Mexico, Halifax, and Brazil. In the United States both American Braille and New York Point are used. In 1909 when the New York City Board of Education decided to establish classes for blind children in the public schools, an investigation was made prior to the adoption of the type in which text-books should be embossed. After several public hearings at which advocates of both New York Point and American Braille spoke the Board selected American Braille as the type to be used.

The development of practical systems of reading for the blind has made possible exceptional results along educational lines. Experience has developed certain principles of pedagogy for the blind which are so well established as to meet with general acceptation.

Principles of Education.—When possible, the education of blind children should begin at an early age. The special disability must be counteracted when the child is young in order that the habits of inactivity which would ordinarily result may not become too firmly fixed. At no stage of life are the blind really helped by doing everything for them—their salvation depends upon the self-reliance which they can develop. Children should be encouraged to do everything within their power and any tendency toward commiseration should be scrupulously avoided.

Definite efforts should be made to develop the intact sensory faculties, especially the tactile sense. This is no more acute in the blind than in sighted children and only becomes so by practice in observation through it. In education the blind child must, of course, first be taught the elements of speech. His education will then proceed according to much the same methods as are employed with seeing children with the single exception that he will need special instruction with reference to the objects of nature and everyday life—matters of visual experience to the average person. Once a blind child is taught the methods of observation he will constantly accumulate useful knowledge of various kinds.

Some sort of physical exercise should be regularly provided for as their tendency will normally be sedentary. This is necessary if they are to retain the health and strength necessary to bring their mental powers to their full fruition. In schools for blind children a gymnasium is an essential and a flat outdoor field for exercise and games is highly desirable.

It is now regarded as an unquestioned principle that the training of the blind, at least after the adolescent period, should not be coeducational. Unless this is observed there are liable to grow up friendships which will result in marriage. This is highly inexpedient for two reasons. In the first place the couple may become hopelessly dependent and it is further thought that there is a risk of the offspring of congenitally blind persons being born blind. Single blind persons have a better opportunity for self-support than do a blind couple, while if the blind man or woman eventually marries a seeing helpmate, as

is often the case, the situation is vastly improved. In the education of the blind, since segregation of the sexes is so general, it should be brought to the physician's attention that homosexual tendencies are liable to develop and should be guarded against in every possible way.

During the course of primary education the ultimate object of self-support under a special handicap should be kept in view. To this end subjects cultivating manual dexterity should be given. Up to a certain point, however, the prime aim should be to provide a good general education. A vocational choice should be made absolutely on the evidence of developed abilities and tastes. This choice is of great importance as the problem of occupation is difficult to the blind, som any fields of endeavor being closed to them and their inability to see proving a handicap —even though a small one—in almost any line of work. Some of the occupations which have been found especially suitable will be discussed later.

Employment of Blind Teachers.—The consensus of opinion and experience shows that the best results in institutions are attained by the combined employment of blind and sighted teachers. In some ways blind instructors are at a disadvantage as regards supervision and discipline but there are some circumstances which render them valuable. The advantages have recently been enumerated in England as follows: (*a*) the teacher being blind, realizes the needs and difficulties of the pupils better than a sighted teacher; (*b*) the blind teacher far excels his sighted colleagues in making clear those subjects where the apparatus used is especially adapted for the blind; (*c*) the presence of a blind teacher in the school acts as a stimulating example and inspiration to the pupils. It may be mentioned as empirical evidence on this point that much of the best pioneer work in the education of the blind has been accomplished by blind men and women.

Higher Education.—Many blind persons after completing the courses at schools for the blind are fitted intellectually to receive with profit higher education. There has recently been brought forward the proposition that there should be founded by the federal government a college or university for the blind. The advantages urged for such a project are that a similar scheme has worked well for the deaf, that the financial burden imposed upon a blind person attending a college for the sighted is very considerable and often prohibitive, and that appropriations for such a purpose would be easier to secure than for the alternative plan of subsidies and scholarships in existing universities for the seeing. The disadvantages urged by opponents of the project are that segregation of the blind any longer than possible in special institutions is undesirable, that the blind need experience in dealing and competing with their seeing fellows, and that the establishment of such an institution would render the regular colleges less ready to accommodate the blind. It might be added that there are some successful precedents for the scholarship or subsidy plan. Several State schools for the blind hold scholarships in various universities and the State of New York at present provides an allowance of $300 a year to each blind person in the State pursuing in a satisfactory manner the prescribed studies leading to an academic degree. This money is to be expended for the pay of readers, who thus bring to the blind person the advantages of books in ink print. Throughout the country there are a considerable number of the blind pursuing college courses and some have taken higher degrees both in this country and abroad.

It remains to mention, however, the importance of the social manners and deportment of the blind. The ideal environment for the blind is not among sightless but among seeing persons. There is already some prejudice against their employment and this is sometimes heightened by certain grimaces and mannerisms which they may develop. These can be obviated if attention is given to them during the course of education and the effort made to correct them.

Museum Facilities.—Another means of education for the blind which has been undertaken in New York has been the preparation of special exhibits for their use by one of the museums. The plan is to have the collection changed from time to time to illustrate matters of common interest. For instance at a time when arctic exploration was in the mind of the public the specimens comprised snowshoes, canoes, sleds, and similar articles which the blind visitors were at liberty to handle and study. This is a field of comparatively recent development but will probably be susceptible of wider extension.

Correspondence Courses.—Several years ago the Illinois School for the Blind inaugurated some correspondence courses open to blind persons in the State. These courses are designed, first, for those who lose their sight too late in life to permit their going to a school, and secondly, for graduates of the institution who wish to pursue their studies further.

Athletics for the Blind.—For the promotion of physical exercise for the blind there has been formed the National Athletic Association of Schools for the Blind, the membership of which embraces sixteen schools. A good idea of the abilities of the blind in competitive athletics can be gained from a list of the standard events which are contested. *For boys,* Senior: twelve pound shot-put, standing broad jump, standing high jump, three standing jumps, running broad jump, fifty-yard dash, and seventy-five-yard dash. Intermediate: fifty-yard dash, eight-pound shot-put, and running broad jump. Junior: fifty-yard three-legged race and fifty-yard sack race. *For girls,* Senior: standing broad jump, standing high jump, thirty-five-yard dash, fifty-yard dash, two hundred-yard relay race, and baseball throw. Junior: fifty-yard three-legged race, fifty-yard sack race, and fifty-yard egg race.

Occupations.—There are a great many lines of occupation open to the blind, dependent upon individual capabilities. Almost any field of activity is open to the blind person of extreme brilliance and power but there will be considered here only the professions and occupations which have proved of general value.

Music.—In its various branches music often proves an excellent profession for the blind. It is a fallacy to suppose that the blind have more musical talent than the seeing. Musical training is given, however, in most of the schools for the blind and latent abilities are thus discovered. Instruction should not be carried to an advanced stage, however, unless there is promise of real talent, and even in such cases the training should be most thorough. Preparation can be made for orchestral positions, pianists, organists, and music teachers. In various schools for the blind arrangements are made to secure tickets for concerts and operatic performances so that the pupils may have the best musical advantages as an aid toward cultivating their taste.

Piano-tuning.—An allied occupation, open to the blind is piano-tuning, and one which is largely practised by them at the present time. The pioneer in this field was a blind man named Montal who was attending the school at Paris. With another pupil he attempted to tune a piano at the school and, though discouraged at first, finally succeeded. He was given charge of tuning all the pianos at the school and instruction was also given to the other pupils. Montal overcame the prejudice against his work after leaving the institution, earned the commendation of the best musicians in Paris, and finally went into the manufacture of pianos. In order to do good work in this field a long and thorough training is necessary so that

the blind tuners can compete on advantageous terms with those who see. There are several piano factories in Germany where only blind tuners are employed.

Massage.—For a long time this occupation has been practised by the blind in Japan, where up to recent years they had a practical monopoly. Even now ninety per cent. of the massage operatives are blind. The work was introduced in England and the Institute for Massage by the Blind was started in London, and the occupation has recently been followed fairly extensively in the United States. The work being wholly dependent upon touch it is evident that it is within the capacity of the blind who make as competent masseurs or masseuses as sighted persons. Some are employed by physicians, some work in hydrotherapeutic establishments, while others are in private practice for themselves. The work has many advantages; it requires no apparatus or machinery, it is lucrative, and it does not require institutional residence, the blind person being able to pursue it while living at home. In the United States a course of training for this occupation is offered by the Philadelphia Orthopedic Hospital and Infirmary for Nervous Diseases.

Fig. 679.—The Practice of Massage by the Blind. From a Japanese Print

Hand-weaving.—This was undertaken as an occupation for the blind in 1904 by the Massachusetts Commission for the Blind. Blind persons are entirely capable of operating the hand-looms needing only a small degree of sighted supervision in order to provide attractive patterns. It is worthy of note, however, that the blind workers have themselves developed many designs of considerable merit. The chief problem is not the execution of the weaving by the blind, but the securing of a market for the work. The product, however, has a fairly wide possible sale among those interested in craftsmanship. Along a similar line it is also possible for the blind to weave rag carpets and rugs.

The Cleveland Society for Promoting the Interests of the Blind has also taken up hand weaving and as a result of their experience certain conclusions were reached. As these may be of interest they are given here: (1) No part of the average operation of weaving is impossible to the average blind person. (2) A blind person may become so accurate in memorizing the design and so adept in the plain-weaving as to earn a fair living wage. (3) Weaving, as a mechanically repeated process, may, and usually does, become an occupation of large interest and pleasure to the worker, a blind person getting a distinct sense of pleasure from feeling the contour and texture of the design. (4) As the value of any hand work as a permanent occupation must depend finally upon the demand in the market, it is essential to know that, in the estimation of those who have kept closely in touch with the movement for handicraft in various lines, the demand is steadily increasing for handmade articles with a regularity which is not to be confused with the spasmodic fad for machine imitations of the same.

Making Willow-ware.—This trade which has met with such success abroad has not worked out very well in the United States owing to the difficulty of securing the raw material of good quality at a reasonable price. In Wisconsin they have grown the willow for themselves and so have avoided this difficulty—in other localities, however, this has not been the case.

Hat-frame Making.—This trade has been developed principally at the Illinois Industrial Home for the Blind in order to provide a useful occupation for blind women. Knitting, crocheting, and bead work were tried but were abandoned because there was no legitimate commercial demand for the products. In the making of wire hat-frames the work was slow at first but speed was soon acquired. It was found that simple machines admirably adapted to operation by the blind were used in the commercial manufacture of frames and ten such machines were installed. The women have been able to do the work either by hand or machine and it has been possible

to dispose of the frames so that the blind operatives can earn very fair wages.

Farm-work.—In view of the fact that agriculture is the most important single industry in the country workers with the blind have devoted thought to the possibility of education in farm-work. In at least two institutions work along this line has been started. The Missouri School for the Blind recently reported that "a class of nine boys and eleven girls is being taught chicken raising. Pupils are assigned the care of the chickens for a definite period, making records of feeding period and amounts, results, and other data, so that they may have practical experience. Instruction is also given in bee-keeping, the parts and construction of the hive being explained in detail." Farm-work offers great promise for the partially blind and for the totally blind of limited mental endowment.

Typewriting and Stenography.—One of the most popular lines in which instruction may be given to blind young men and women of good mentality and fair education is stenography and typewriting. There has been devised a key machine by which stenographic notes may be recorded on a ribbon. By reading this ribbon the notes may be transcribed on the typewriter with a high degree of accuracy. This work is pleasant and where employment can be secured the wages are very desirable. It is needless to say that for pupils of considerable intellectual capacity, this occupation offers much more interest than a purely manual trade.

Telephone Operating.—This has been found a possible occupation for blind girls, particularly on small private switchboards. It is probably impractical at large central offices.

Provision for the Blind.—At the present time there is comparatively adequate provision for the needs of the blind in comparison with those of other classes of the physically handicapped. All civilized countries care for many of their sightless in one way or another and in most cases the methods accord with modern principles of work.

Associations.—There is an American Association of Workers for the Blind which meets each year in a convention generally held at one of the schools for the blind. The American Association of Instructors of the Blind also convenes in an annual meeting. The American Library Association has a committee on work with the blind and the National Education Association deals with questions affecting the instruction of the blind. There are also, of course, a great many State and local associations of blind persons and of those working in their interest.

An International Conference on the Blind is held triennially in different countries. Among the large associations abroad are the Association Valentin Haüy in France and the British and Foreign Blind Association in England.

United States.—In the United States there are a large number of institutions and organizations for the benefit of the blind. The national government makes an annual appropriation of $10,000 as a subsidy for the manufacture of embossed books and literature, the reading matter manufactured under this grant being distributed to the various State schools for the blind. New York State also makes an annual appropriation of $2,000 for the same purpose. The distinguishing feature of provision in the United States is that the public authorities have to so great an extent assumed the responsibility of assisting the blind, who, therefore, receive their education, not at the hands of private philanthropy, but as a right of their citizenship in the community. The work is thus considered in the category of general public education. Every State in the Union now provides for the education of the blind. There are, of course, many other institutions, some of them among the best which are supported by private endowment or charitable contribution.

The Perkins Institution and Massachusetts School for the Blind is the institution of earliest foundation, 1829. The New York Institution for the Blind was started in 1831 and the Pennsylvania Institution for the Blind was founded in 1833 in Philadelphia, whence it has since moved to Overbrook. Ohio inaugurated a State school in 1837. Since that time all the other States have made provision for the blind.

There are fairly extensive library facilities for the blind. In order to encourage the distribution of embossed literature free mail transportation is provided by the federal Post-office Department. The *Matilda Ziegler Magazine* issued in two styles of embossed type is supported by a private benefaction and is sent without charge to every blind person desiring it.

An interesting development of recent years is the provision in the public day schools for blind children. Special classes and teachers are set apart and in many instances the blind children are transferred as soon as possible to the classes for the sighted. The same text-books as are utilized by the seeing children are provided in embossed type for the blind pupils and the instruction thus progresses on the same basis. In New York these books are in American Braille, that type having been adopted after extended hearings on the merits of the respective systems.

The general educational work, however, in its various phases is directed especially toward the training of blind children who have not passed the receptive or plastic age. In addition to the regular curriculum there is also provided industrial training of one type or another so as to render them self-supporting later on. With older blind persons, however, the employment problem is all important. With a view to solving this there have been established in several States trade schools and workshops for the blind. An example of such provision is in Massachusetts where the work done by the blind is known throughout the State.

Five States, Massachusetts, Ohio, New Jersey, Illinois, Delaware, and Utah, have State commissions for the blind. The duty of these bodies is to look after the welfare of the blind both educationally and industrially. In two instances very active propaganda for the prevention of blindness have been inaugurated by these commissions. Unfortunately a legislative enactment creating a commission in New York State has recently (1912) been vetoed by the governor at the behest of private interests. Maryland maintains a State workshop for the blind.

State care of blind babies is provided in the States of New York, New Jersey, and Arizona. In New York the Commissioner of Education may appoint as pupils to any one of a number of specified educational homes blind babies or children. For their board and care the State pays one dollar a day. The State of New Jersey pays $330 a year for the maintenance of blind babies which it commits to a certain home. The State of Arizona has made provision for the payment of a stipend of one dollar a day for the proper care and education of blind babies and children under school age. It might also be pointed out that Connecticut maintains a kindergarten and nursery in conjunction with the State institution for the blind. There are also other private nurseries throughout the country, probably the most notable one being in Boston.

Industrial Establishments.—The principal industrial establishments for the blind in the United States are here designated together with a notation as to the products turned out of the shop. Workshop of the Perkins Institution for the Blind, Watertown, Mass., mattresses, pillows, door mats, and chair caning; Workshop of the Maryland School for the Blind,

Baltimore, Md., brooms, mattresses, and chair caning; Working Home for Blind Men, Philadelphia, Pa., corn brooms, rag carpet, and chair caning; Industrial Home for the Adult Blind, Oakland, Cal., brooms, hammocks, mattresses, chair caning, broom sacks, and fancy work; Institute for the Blind, Hartford, Conn., brooms, chair caning, fancy work, and mattresses; Industrial Home for the Blind, Brooklyn, N. Y. corn brooms, chair caning, mattresses, and hammocks; Industrial Home for the Blind, Chicago, Ill., brooms; Industrial Home for Blind Men, Indianapolis, Ind., brooms; Polytechnic Institute for the Blind, Washington, D. C., ink printing; Clovernook Home for the Blind, Mt. Healthy, near Cincinnati, O., weaving, baskets, crochet and knitting work; Workshop for the Blind, Milwaukee, Wis., basket specialties in willow and rattan; Michigan Employment Institution for the Blind, Saginaw, Mich., brooms, caning, cobbling, piano tuning, feather dusters, carpets, rugs, and baskets; Society for Promoting the Interests of the Blind, Cleveland, O., cotton and linen draperies, caning chairs; Workshop for Blind Men, New York City, brooms, caning chairs; Industrial Department of the Massachusetts Commission for the Blind, Cambridge and Pittsfield, Mass., rugs, art fabrics, a special mop known as the *Wundermop* invented in and made exclusively by these shops, brooms, mattresses, caning, and fancy work; Broom Shop, Buffalo, N. Y., brooms.

Great Britain.—The first institution for the blind in Great Britain was founded through the efforts of Edward Rushton, himself blind, in 1791. This was the Liverpool School for the Indigent Blind. This was followed soon after by the Royal Blind Asylum in Edinburgh which opened its doors in 1793. Others followed in quick succession: British Asylum, 1793; School for the Indigent Blind, Leatherhead (formerly at Southwark), 1799; Norwich Asylum and School, 1805; Richmond Asylum, Dublin, 1810. The Royal Normal College and Academy of Music for the Blind, Upper Norwood, was founded in 1872.

England and Wales.—In 1907 according to Sir Francis Campbell there were twenty-four resident schools and forty-three workshops for the blind in addition to the day classes for blind children maintained by the public school authorities in almost every city of reasonable size. At the same time there were forty-six home teaching societies. All of these societies lend books in tactile print and a good many public libraries make similar provision.

The British and Foreign Blind Association is one of the largest organizations for promoting the interests of the blind, through education, employment, and the distribution of books. The International Lending Library in London sends embossed books to all parts of the Kingdom. There are also fourteen magazines published in embossed type. There are thirty-six pension societies. The Gardner Trust is a large foundation with a purpose of instructing the blind in music, trades, and professions; it also makes grants for special purposes.

Scotland.—A unique feature of work for the blind in Scotland is the Outdoor Mission. Twenty-four missionaries or teachers are employed in addition to a large number of volunteers and the blind are visited throughout all of Scotland. There are several societies with a view of providing work for the blind. There are five schools for blind children and connected with these are workshops for adults.

Ireland.—There are twelve institutions for the blind in Ireland and an Outdoor Mission similar to the one in Scotland. Nine of the institutions are, unfortunately, asylums. There is little manufacturing in Ireland and there is therefore a scarcity of work adapted to the abilities of the blind.

British Colonies.—In most of the British Colonies provision is made by public authorities for the education of blind children and in some cases industrial training is provided at the expense of the State. Embossed literature is carried post free.

In Australia there are institutions for the blind at Melbourne, Sydney, Adelaide, Brighton, Brisbane, and Maylands.

In New Zealand there is an institution at Auckland. In Cape Colony there is an institution at Worcester, established in 1881 and supported partly by government grant and partly by private philanthropy.

In Canada there are schools for the blind at Brantford, established in 1871 and Halifax established 1867. In Montreal there are two private institutions.

Germany.—There are in Germany about thirty institutions. The distinguishing feature of German work for the blind is the extent to which the responsibilty for their education is assumed by the community as a whole. Over half the institutions are wholly supported by the State and most of the remainder derive most of their support from the provinces, the communes, or the State. Only two are private charitable institutions.

Great emphasis is placed in Germany on the after-care of the blind, the schools considering that their responsibility to pupils does not cease with graduation. The blind are therefore assisted to establish themselves in business and local cooperation is secured to help place them on a permanent footing.

Austria.—For blind children there are in Austria eight institutions. Children not accommodated in these institutions are required to be educated so far as possible in the public schools. One of the best-known institutions for the blind in the world is located at Vienna and is under the direction of Alexander Mell.

France.—France is credited with the establishment of the first institution, still existing at the present time, for the relief of the blind as well as with the inception (1785) of the first modern organization for their education—the Institution Nationale des Jeunes Aveugles. There are about thirty schools for the blind, some of which receive national support. Others are maintained by departments, municipalities, and religious bodies. The most important educational institutions in Paris are, besides the one already alluded to, with the dates of their foundation: the École Braille, 1883; Etablissement des Sœurs Aveugles de St. Paul, 1852; and the Etablissement des Frères de St. Jean de Dieu, 1875. The Valentin Haüy Association, named after the illustrious French pioneer in the work, takes a general interest in the affairs of the blind and publishes a magazine, the *Valentin Haüy*, in their interest.

Italy.—The first effort to care for the blind in Italy was made with the establishment of an asylum for the blind "S. Giuseppe e Lucia" in Naples in 1818 in connection with the royal almshouse. Another was founded in Padua in 1838 and one at Milan in 1840. Other institutions for the blind have since been established at Turin, Pavia, Como, Genoa, Reggio Emilia, Bologna, Florence, Assisi, Rome, Palermo, and Cagliari. Practically all the work for the blind in Italy is done by private philanthropy and there are several large foundations. There is a statute providing for the obligatory education of blind children, but it is largely inoperative. Embossed literature in Italian for the blind is still scanty.

Spain.—Work for the blind is not active in Spain. There are fourteen institutions for the blind but some are small and they are mostly in association with asylums for the deaf. There are two each in Barcelona and Madrid. The first institution for the blind in Spain was established at Barcelona in 1820, the next at Madrid in 1842.

Denmark.—The oldest institution in Denmark is the Royal Institution for the Blind which was founded in 1811 on the initiative of Professor Bron-

son. A workshop and home was added in 1825 and in 1857 the institution moved to a new building built for it by the State. In 1861 a preparatory school for blind children under ten years of age was started. In 1862 there was inaugurated a society for the promotion of self-support by the blind. This society cooperates in the work of the Royal Institution and women as well as men are provided for. Director Moldenhawer is in charge of the work.

Sweden.—Before 1879 the education of the blind in Sweden was in conjunction with the instruction of the deaf, but since that date it has been entirely separate. The principal school is the Royal Institution for the blind at Tomteboda, near Stockholm.

Norway.—In Norway, under provisions of the act of July 8, 1881, the State provides for the education of blind children between the ages of nine and twenty-one with a minimum of eight years instruction for each pupil. This automatically imposes on the education authorities the necessity of the maintenance of a sufficient number of schools for the blind.

Finland.—In Finland there are two small schools for the blind, one at Helsingfors established in 1865 where instruction is given in the Swedish and Finnish languages, and one at Kuopio established in 1871 where instruction is given in Finnish only. Both are supported by the State.

The Netherlands.—In Holland there is but one educational institution for the blind, the one located at Amsterdam. Connected with the school is a preparatory department (at Benuchem) and a home for adults. There are workshops for the blind at the Hague, Rotterdam, Utrecht, Amsterdam, and Middleburg.

Egypt.—The only institution for the blind in Egypt is the one at Cairo. Outside of this work there is no provision for the blind in Egypt, a country where blindness is unusually prevalent. The only occupation open to the blind not accommodated in the Cairo institution is religious recitation at services and funerals. Blind women and girls have no occupation whatever. Some time ago there was another school for the blind in Cairo maintained under a yearly grant of $10,000 from the native ecclesiastical authorities. This was taken over by the ministry of education but was finally discontinued. Through the instrumentality of Dr. and Mrs. T. R. Armitage a plan for the education of the blind in Egypt was presented to Queen Victoria in 1900. This was transmitted by the Queen to the Khedive of Egypt who approved the proposals and gave a donation toward the establishment of the Cairo school which was started in 1901.

Trachoma is very prevalent in Egypt, in fact it has often been known as the Egyptian disease. During Napoleon's campaign in Egypt it is said that nearly every soldier in his army contracted this disease of the eye.

Palestine.—The needs of the blind are urgent in Palestine owing to the great prevalence of blindness in that country. Ophthalmic clinics are now provided in most of the cities. There is a home and school for blind girls in Jerusalem which is a development of a day school established in 1896 by a missionary from the United States. There is also a small school at Urfa maintained by an American mission.

India.—Only recently has there been any effort to provide for the blind in India. Some time ago an excellent school for the blind was founded at Amritsar but has since been moved to Rajpur. A government school and hospital for the blind was established in 1903 at Bombay as a memorial to Queen Victoria. Instruction is given in elementary subjects, tailoring, typewriting, carpentry, machine work, and carpet-weaving. There are also small schools at Calcutta, Parantij, Calicut, Coorg, Palancottah, Chota-Nagpur, and Moulmein in Burma. A system of Oriental braille has been devised for use in these schools.

At Bombay there is also an American Mission School for the Blind founded in 1900, and this now accommodates fifty pupils. Instruction is given in both elementary and industrial subjects; considerable attention is devoted to music. Plans are also being laid by the Hindus of Bombay for the erection of a native school.

Japan.—The history of the blind in Japan is of considerable interest as it traces the evolution of the blind from charitable indulgence and support to self-dependence. According to Tadasu Yoshimoto (*Outlook for the Blind*, III, 91), in the year 858, Prince Hitoyasu, son of the Emperor, became blind and many blind men of good standing became his attendants. The Prince divided among them part of his income which was afterward largely augmented and distributed to all the blind in the country. In the year 886 in memory of the Prince blind officers were appointed to look after the welfare of the sightless throughout the Empire. During the early part of the seventeenth century the government increased the tax which had long been levied throughout the country for the benefit of the blind and favored and protected them in every way possible. In 1870, however, when the government began to adopt European customs, the posts of the blind officials and the pensions for the blind were abolished. As a matter of fact this was of indirect benefit to the blind as it made it necessary for them to become self-supporting. Massage and music-teaching became by custom virtual monopolies for the blind.

The first school for the blind and deaf was founded in Kyoto in 1878 and another was started in Tōkyō soon after. At the present time there are in Japan eighteen schools for the blind and twenty-one schools for the blind and deaf, in addition to some public schools where the blind boys and girls are being educated with seeing children. Some embossed books have been published and several embossed periodicals are being issued. Libraries for the blind have been started in Tōkyō and elsewhere. Only recently the government authorized the Education Department to erect a model school for the blind in Tōkyō.

China.—The complicated system involved in the writing of the Chinese language brings up several special difficulties in the instruction of the blind. A numerical method of representing the sounds of the language was devised by W. H. Murray, but about the merits of this system there has been some difference of opinion. A braille code for the Mandarin dialect has been arranged by Miss Garland of the China Inland Mission. There is a school for the blind at Peking, and at Foochow a large school for blind boys and girls, maintained by the Church Missionary Society. Provision for the education and care of the blind is made by missionaries at Canton, Ningpo, Amoy, and Fukien.

In 1900 an analytical census of the blind was taken in conjunction with the national census. The regular enumerators made only an informal report giving the names and addresses of persons supposed to be blind. Correspondence with these persons was then instituted in order to ascertain further and more complete details. The lists of names compiled have been of much value in State work.

The final report of this national census showed there to be 64,763 blind persons in the United States, but the correct figure is probably somewhere between eighty and one hundred thousand. Many of the persons corresponded with did not reply and there were probably others missed in the preliminary enumeration. Of the number reported 35,645 were reported as totally blind, and 29,118 as partially blind; 37,054 were male and 27,709 female; 45,479 were native-born whites, 10,694 foreign-born whites and 8,228 colored. The age distribution was as follows:

Age.	Total number.	Number per million population of same age.
10 years or under	2,307	128
10–19 years	6,001	384
20–29 years	4,861	351
30–39 years	5,024	478
40–49 years	6,504	845
50–59 years	8,530	1,655
60–69 years	10,507	3,396
70–79 years	11,421	8,136
80–89 years	7,409	*
90–99 years	1,596	*
100 years and over	232	*
Age unknown	290	*

* Percentages unreliable.

STATISTICS.—In the accompanying table are given the numbers of the blind in various countries in absolute figures and in relation to the total population.

DOUGLAS C. MCMURTRIE.

LITERATURE.

The literature regarding work for the blind is very unsatisfactory. There is no good history of their education. The best material can be gleaned from periodicals, among the best of which is the *Outlook for the Blind*, Boston. The *Encyklopädisches Handbuch des Blindenwesens* by Alexander Mell is also of great value. The article on *Blindness* in the *Encyclopædia Britannica*, 11th Edition, iv., pp. 59–72, is the best short review of the subject.

THE BLIND.

ABSOLUTE AND RELATIVE NUMBERS FROM LATEST OFFICIAL DATA.

Country.	Date.	Number of blind.		Authority.
		Individuals.	Per million inhabitants.	
United States*	1900	35,645	469	Special report of the Census (1906) *The Blind and the Deaf.*
Canada	1901	3,279	610	British Empire Census, 1901; "Report with Summary and Detailed Tables," published 1906, page 69.
Newfoundland and Labrador	1901	225	1,018	British Empire Census, 1901.
Trinidad	1901	512	1,870	British Empire Census, 1901.
Chile	1907	2,601	800	Censo de 28 Noviembre, 1907, page 307.
Mexico	1900	12,959	952	Censo de 28 Octubre, 1900; Resumen General, page 78.
Ireland	1901	4,253	954	British Empire Census, 1901.
Scotland	1901	3,253	727	British Empire Census, 1901.
England and Wales	1901	25,317	778	British Empire Census, 1901.
Belgium*	1906	3,076	434	*Annuaire Statistique*, 1908, page 27.
Netherlands*	1909	2,710	462	*Jaarcijfers voor het Koninkrijk*, 1910, page 27.
Denmark	1901	1,047	427	*Statistisk Aarbog*, 1911, page 15.
Norway	1910	2,097	889	*Statistisk Aarbog*, 1911, page 15.
Sweden	(about 1900)	3,413	664	*Statistisk Tidskrift*, 1910, page 11.
Germany*	1900	34,334	609	*Statistisches Jahrbuch für das Reich*, 1908.
Switzerland	1895	2,107	722	*Enc. Brit.*, 11th Edition, iv., page 60.
France	1901	27,174	698	*Annuaire Statistique*, 1906, page 8.
Portugal	(about 1900)	5,650	1,040	*Enc. Brit.*, 11th Edition, iv., page 60.
Spain	1877	24,608	1,006	*Enc. Brit.*, 11th Edition, iv., page 60.
Gibraltar	1901	33	1,200	British Empire Census, 1911.
Malta	1901	418	2,011	British Empire Census, 1911.
Italy	1901	38,160	1,175	*Censo della Populazione*, 10 Febbraio, 1901, ii., page 344.
Austria*	1905	14,052	515	*Statistisches Handbuch*, 1907, pages 52–53.
Hungary	(about 1900)	19,377	1,006	*Official Publication* (Magyar).
Servia	1900	2,345	941	*Annuaire Statistique*, 1906, page 96.
Bulgaria	1905	5,319	1,318	*Annuaire Statistique*, 1910, page 114.
Roumania	1899	4,967	834	*Denombrement de Dec.*, 1899, *Résultats Définitifs.*
Poland (Russian)	1897	7,005	745	Census, 28 Jan., 1897; St. Petersburg, 1905, ii., page 186.
Finland	1900	3,229	1,191	*Befolkningsstatistik No. 37: Aperçu de la population de la Finlande au.*, Dec., 1900.
Russia (in Europe)	1897	215,413	2,097	Census, 28 Jan., 1897; St. Petersburg, 1905, ii., page 196.
Siberia and Central Asia	1897	25,482	1,887	Census, 28 Jan., 1897; St. Petersburg, 1905, ii., page 186.
Cyprus	1901	1,732	7,300	British Empire Census, 1901.
Egypt*	1907	148,280	13,250	Census of 1907, page 158.
Cape Colony	1901	2,802	1,163	British Empire Census, 1901.
Ceylon*	1901	3,747	1,050	British Empire Census, 1901.
British India	1901	354,104	1,207	British Empire Census, 1901.
Java	1905	45,837	1,523	*Jaarcijfers voor Kolonien*, 1908, page 18.
Australia and Tasmania	1901	2,744	727	British Empire Census, 1901.
New Zealand	1901	390	504	British Empire Census, 1901.

* Relates specifically to the *totally* blind.

Blindness.—(Lat., *Cæcitas;* Ger., *Blindheit;* Fr., *Aveuglement.*) *Amaurosis* is sometimes used synonymously with blindness, and in selected cases—the cause of which is obscure, or is located in the nervous apparatus—this is admissible, with the same limitations that apply to blindness. Blindness is a misleading term, being a symptom only, and should not be used in scientific language (except in a generic sense) without a qualifying phrase which describes the condition upon which it depends—as blindness from optic-nerve atrophy. A strict application of the term would include only such eyes as are not possessed of light perception. It is, however, usually understood to embrace all eyes incapable of recognizing the outline or shape of objects; and practically it should include all eyes with vision less than $\frac{1}{200}$, *i.e.* all eyes which are able to count fingers at only one foot, for such individuals have to be *led* around.

Economic Effects of Blindness.—Blindness is a misfortune not only to the individual, but to a community, for a blind person has to be *supported,* and, too, he is not a *producer.* To illustrate the importance of these two factors, let us apply them to the United States, which, according to the census of 1900, had 64,763 blind inhabitants. The *cost* of supporting one blind person in an economical manner may be placed at $132 annually ($2 per week for board, $28 for clothing), so that the *cost* to this country for caring for its blind is $8,542,716 annually. The *producing* capacity of a man at $1.20 for each working day and of a woman at $0.40 a day would be $404 and $256 respectively annually, which would give $22,063,300 as the annual earning capacity lost to this country by its blind—cost and loss together amounting to $30,606,036.

The cost of living and wages have both increased since these figures were adopted and hence the community is a loser to that extent. If the increase in the cost of living be placed at twenty per cent., and of wages at ten per cent., $3,908,873 should be added to the cost of the blind to the United States, which would bring the total $34,514,909—and yet this is not exact, for a certain number of blind persons are wage earners.

The *geographical distribution* of blindness as shown in Table I., compiled by Mayr, of Munich, in 1877, has been subject to slight changes by later statistics, so far as the proportion of the blind to the population is concerned.

Table I.

Country.	Population.	Total number of blind.	Number of blind in 10,000.
England and Ireland	31,631,212	31,159	9.85
Denmark	1,864,496	1,465	7.86
Norway	1,701,756	2,320	13.63
Sweden	4,168,525	3,359	8.06
Finland	1,732,621	3,891	22.46
Austria	20,394,980	11,329	5.55
Hungary	15,417,327	18,523	12.01
Switzerland	2,669,147	2,032	7.61
Netherlands	3,575,080	1,593	4.46
Belgium	4,529,560	3,675	8.11
France	36,102,921	30,214	8.37
Spain	15,658,531	17,379	11.26
Italy	26,413,132	26,826	10.16
United States of America	38,558,371	20,320	5.27
Argentine Republic	1,743,199	3,529	20.24
British colonies in			
North America	583,535	361	6.19
West Indies	905,730	2,030	22.41
Africa	330,460	416	12.53
Australia	305,730	116	3.79
Germany	39,862,133	35,048	8.79
Totals	248,148,446	215,585	8.74

The population of the United States in the above table is taken from the census of 1870. The census for 1880 shows a population of 50,155,783; number of blind, 48,928; number of blind in ten thousand, 9.73. A striking difference is the great increase of blindness in the United States in the subsequent decade, as is shown in the figures for 1880. Various causes must be considered in determining the reasons for this increase in blindness, the most important of which are the following: 1. The census returns were more complete for the last census than they have been heretofore. 2. Injuries more or less remote from the eye, sustained during the late war, continue to swell the ranks of the blind, and with pensions in view a considerable number make the claim unjustly. 3. The foreign element in our population adds to the percentage of blind; for natives of the United States furnish 9.13 blind to 10,000 inhabitants, while 13.45 blind are found in the same number of our foreign population. 4. The increase of manufacturing interest and its spread to localities remote from competent professional care. 5. The increase of those competitive trades that bring bodily and mental strain, which are liable to produce changes in the nervous system, in which the eyes participate.

The next decade—census of 1890—shows a gratifying reduction in the proportion of blindness: population, 62,622,250; blind, 50,411; number of blind in 10,000, 8.1; number of natives blind in 10,000, 7.4; number of foreigners blind in 10,000, 10.1. This improvement is due to two causes: first, the proportion furnished by the late war has been depleted by death, and the proportion of foreigners has been lessened by laws restricting immigration; second, people are being educated to seek proper relief for diseases and injuries of the eyes.

The report for 1900 shows a population 75,994,575.

Number of blind, 64,763; number of blind in 10,000, 8.5
" " native blind, 45,479; " " " " " 8.0
" " foreign " 10,604; " " " " " 10.4

The slight increase here shown is doubtless due to the increase in the competitive trades and mechanical work, with the attendant dangers to the eyes.

The latest foreign statistics, as obtained from Prenzing, Medical Statistics, Jena, 1906, show the number of blind to 100,000 inhabitants of the countries referred to, as follows:

Table II.—The Number of Blind in 100,000.

Country.	Year.	Men.	Women.	Average.
Prussia	1900	64	56	61
Saxony	1900	60	60	63
Wurtemburg	1900	66	54	60
Baden	1900	57	50	54
Austria	1830	86	75	81
Hungary	1890	102	104	106
Switzerland	1895	78	66	72
Netherlands	1899	51	43	47
Belgium	1878	98	64	81
Italy	1877	172	122	147
Portugal	1878	210	191	200
England and Wales	1901	84	73	78
Scotland	1901	77	69	73
Ireland	1901	97	94	95
Denmark	1901	66	47	57
Norway	1893	135	123	129
Finland	1890	113	196	156
Russia (Europe)	1886	190	200	195
Siberia	1890	142	115	129
U. S. A.	1890	88	77	81
India	1901	121	120	120
Ceylon	1901	119	89	105
New Zealand	1901	101	73	87
Bulgaria	1888	344	285	315
Argentine Republic	1869	213	191	202
Cape Colony	1901	124	108	116
Trinidad	1901	185	189	187

The *climatic influence*, as illustrated in Europe, is shown in Table III., from Magnus, of Breslau, 1883.

TABLE III.

Between latitudes 30° and 40° the number of blind in 10,000 is 11.09.
Between latitudes 40° and 50° the number of blind in 10,000 is 8.63.
Between latitudes 50° and 60° the number of blind in 10,000 is 7.55.
Between latitudes 60° and 70° the number of blind in 10,000 is 18.04.

And for the Western continent the same author gives Table IV.

TABLE IV.

Between latitudes 10° and 20° the number of blind in 10,000 is 22.41.
Between latitudes 20° and 30° (vacant).
Between latitudes 30° and 40° the number of blind in 10,000 is 8.96.
Between latitudes 40° and 50° the number of blind in 10,000 is 5.36.

According to the U. S. Census Reports for 1900 the three grand divisions of this country show:

Atlantic Division, number of blind to 10,000 inhabitants..... 8.3
Central Division, number of blind to 10,000 inhabitants..... 9.0
Western Division, number of blind to 10,000 inhabitants.... 5.0

The small number of blind in the Western Division is probably due to the fact that a large number of its inhabitants represent the healthy, able-bodied settlers from other States; that there are fewer manufacturing industries; and that there are fewer foreigners and negroes within the borders.

The hot southern latitudes are injurious, because of their dry, sandy interiors (in which the glare and the prevalence of high winds, accompanied by clouds of a fine sandy dust, exert an irritating influence upon the eyes), and their moist, swampy, miasmatic borders and water-courses. The cold northern latitudes are injurious, because confinement in badly ventilated quarters is a necessary concomitant; and, the days being short during the long winters, the work of the eyes is crowded into a limited time, or is prolonged in insufficiently lighted rooms, where work becomes injurious. The most temperate zone presents the least number of these objections, hence we find here the smallest percentage of blindness. There are also geological causes which influence the percentage of blindness; for instance, it is more frequent on one side of the Jura Mountains than on the other.

It has been asserted that blindness was more frequent in cities than in rural districts, and this, aside from such causes as lead to blindness from injuries, trades, etc.; but investigations in Russia, and by Howe in this country, would seem to refute that claim under the present existing circumstances. Investigation of the number of blind in cities of the United States containing 50,000 and upward inhabitants showed that the proportion was thirty-three per cent. less than in the country; and still further investigation by Howe seemed to show that this improvement was due to the more general use of preventive measures against ophthalmia neonatorum in cities than by the country practitioners.

That there are *race peculiarities* is shown by the fact that out of 10,000 Christians there are only 9.4 blind, while the same number of Jews furnishes 13.3 blind. One reason for this large percentage of blindness in Jews is the great frequency with which they suffer from glaucoma. It is said that the sclera is more dense and less elastic in people of this race than in others, and that this condition favors the development of glaucoma. It has been further claimed that dark eyes are more prone to amaurotic affections than light ones, and that Jews, who usually have dark eyes, are therefore more liable to suffer from blindness. This, however, is not borne out by facts, for dark races are usually possessed of deeply pigmented eyes, yet the percentage of blindness is not great with them. It should be remembered, however, that the so-called amaurotic affections constitute but a small proportion of the causes of blindness; and the fact should not be overlooked that overcrowding and bad ventilation are often found in the class to which the majority of Jews belong—and such surroundings are prolific sources of external inflammations of the eye. Consanguinity in marriage is another cause which renders the Jewish race more prone to blindness than others. They, too, almost invariably live in cities, where the percentage of blindness has heretofore been higher than in rural districts. The number of blind negroes in the United States in 1900 was 8,228 out of a population of 8,833,994, or 8.9 to 10,000. Lack of care for diseases and injuries is the probable cause of much blindness with them, rather than any other racial difference. The number of blind native-born Americans is 8.0 per 10,000 inhabitants. The number of foreign-born blind in America, per 10,000, is 10.4.

Influence of Sex.—The United States, according to the Census Reports for 1900, has a population of 38,816,448 males, and 37,178,127 females, which gives a preponderance of 1,638,321 males. The number of blind males is 37,054, and of females, 27,709—which gives a preponderance of 9,324 blind males—or 9.5 males, and 7.4 females, to the 10,000 inhabitants. This difference is a slight one, and can be easily accounted for by the accidents arising from exposure of the eyes to the injurious influences of the trades followed by men. An interesting fact bearing upon this point is the comparative diminution in the percentage of blindness in males after they reach an age which recalls them from pursuits that endanger the eyes to surroundings more nearly like those of females. Table V., prepared by Magnus from the Prussian census, illustrates this condition most aptly.

TABLE V.

Age.	Number of blind, 1871.		Number of blind, 1880.	
	Males.	Females.	Males.	Females.
Under 10 years	664	558	572	488
10 to 20 years	1,113	845	992	823
20 to 50 years	2,572	3,336	3,565	2,989
Over 50 years	5,752	7,100	6,148	6,975

See in this connection Table X. for the causes which produce blindness at different ages.

TABLE VI.

Age	Percentage of blind between the ages given.	Percentage of population.	Number of blind in 10,000.
1 to 10 years	3.7	24.9	1.75
10 to 20 years	4.6	19.9	2.36
20 to 30 years	9.8	16.4	3.25
30 to 40 years	11.1	13.0	3.81
40 to 50 years	15.2	11.1	6.84
50 to 60 years	17.3	7.5	11.50
60 to 70 years	19.7	4.7	26.23
70 to 80 years	13.5	1.8	92.44
80 to 90 years	4.3	.3	207.00
90 to 100 years	.27	.02	373.20

Table VI. gives the percentage of blind *of* different ages in column 2, and the percentage of population *at* different ages in column 3 (Katz), while column 4, which has been adapted from Meyr's table, shows the number of blind in 10,000 *at* different ages.

This table, which is a very interesting and instructive one, deserves attention for its own merits; yet it becomes more instructive when considered in connection with Table X., which gives the causes that produce blindness at different ages.

The following table from Eulenburg's *Real-Encyclopädie*, p. 505 (1894), shows the percentage of blindness at different ages in the countries referred to, as follows:

Table VII

Ages.	Thirteen German States.	England, Wales, and Ireland.	Finland.	Netherlands.	Belgium.	United States.
1 to 5....	1.45	1.61	1.70	0.69	0.47	0.58
6 to 10....	2.63	2.30	2.39	1.00	.79	1.66
11 to 15....	2.42	3.23	3.21	.98	1.60	2.75
16 to 20....	3.73	3.76	4.30	1.92	1.87	3.38
21 to 30....	4.40	5.12	17.00	1.93	3.19	3.30
31 to 40....	6.41	7.81	12.52	2.95	5.51	4.17
41 to 50....	9.90	10.95	126.31	4.31	14.11	6.55
Over 50....	33.18	37.39	103.49	16.59	25.85	23.73
Not stated.	50.82	13.27	19.31	12.76	..	13.56

Influence of Consanguinity of Parents.—Of 2,527 blind persons whose parents were cousins, 39.3 per cent. had blind relatives; 5,389 whose parents were not related showed 17.6 per cent., only of blind relatives (U. S. Census Reports 1900).

Influence of Occupation.—The causes of blindness incidental to occupation may be divided into two classes, viz., *traumatic* and *onn-traumatic.*

Traumatic.—Under this head are included such occupations as necessitate exposure of the eyes to the direct influence of injurious agents from without, which result from the work performed—as machinists, who are constantly exposed to flying bits of metal, which often produce injury of the eye and blindness; and the same is true of blacksmiths, locksmiths, stonecutters, and miners. The last named are also exposed to the dangers of premature or careless explosions. Cases of *monocular blindness* almost invariably arise from the causes just considered.

Cohn found 535 men with 554 blind eyes, and 241 women with 446 blind eyes. Preference is shown for neither eye. The United States census reports for 1890 (there were no tables on this subject in the 1900 report) show 93,988 cases of monocular blindness—or 15.1 to 10,000. The males show 21.7 to 10,000; females, 8.3 to 10,000. The greater frequency of binocular blindness in females is another argument in favor of the accidental occurrence of blindness from the injurious trades followed by men.

Non-traumatic. — Under this head are included such occupations as produce blindness indirectly—as myopia, from over use of the eyes. Professional men, whose duties necessitate much study; and others, who, from necessity or preference, do much reading, or much fine work, which requires close and long-continued use of the eyes, are liable to suffer from myopia and the train of symptoms which in this disease lead to blindness. Workers in lead are liable to suffer from neuroretinitis or atrophy of the optic nerves; and workers in India rubber are exposed to the same dangers, from sulphide of carbon. It is claimed that optic-nerve atrophy sometimes occurs in workers who are exposed to the fumes of tobacco or of alcohol. Soldiers in crowded barracks are apt to suffer from conjunctival diseases, and the exposure to wind, dust, glare, and inclemencies of weather, when marching, may also cause the same trouble. Sailors who are constantly exposed to the vicissitudes of weather are liable to suffer from conjunctival and other forms of eye disease, and their crowded quarters and often meager fare are also conducive to eye affections.

Causes of Blindness.—Table VIII. gives an *anatomical* grouping of the causes of blindness, compiled by Magnus from 770 cases.

Table VIII.

	Per cent.
Conjunctiva	16.364
Cornea	10.650
Uveal tract	22.208
Retina	16.259
Optic nerve	22.597
Glaucoma	12.597
Congenital deformities of the eyes	2.468
Unclassifiable	2.857

Table IX., compiled by the same author from a study of 2,599 cases reported by various writers, gives the causes of blindness, arranged in *pathological* groups, and the percentage of each individual cause.

Table IX.

A.—*Congenital blindness.*	Per cent.
Anophthalmus and microphthalmus	1.068
Megalophthalmus	.435
Congenital cataract	.119
Choroiditis, congenital	.158
Atrophy of optic nerve, congenital	.751
Retinitis pigmentosa congenitalis	.751
Congenital blindness with retinal atrophy	.079
Congenital tumors	.039
Congenital amaurosis, not specified	.237
B.—*Acquired blindness*—(*a*) From idiopathic diseases of the eye.	
Ophthalmia neonatorum	10.876
Trachoma and blennorrhea of adults	9.492
Diphtheritic conjunctivitis	.356
Diseases of the cornea	8.068
Iridochoroiditis, cyclitis, iritis	8.860
Choroiditis myopica	.949
Choroiditis, choroido-retinitis	1.107
Retinitis pigmentosa, acquired	1.266
Retinitis apoplectica	.119
Neuroretinitis	.791
Detachment of retina	4.746
Glaucoma	8.978
Idiopathic optic-nerve atrophy	7.751
Tumors of the eye and its surroundings	.356
Unclassifiable	3.368
C.—*Acquired blindness*—(*b*) Injuries	
Direct injury of the eye	4.034
Unsuccessful operations	1.938
Injuries of head	.277
Traumatic sympathetic ophthalmia	4.509
D.—*Acquired blindness*—(*c*) The eye disease being in consequence of disease of the body.	
Diseases of the eye from syphilis	.470
Gonorrheal conjunctivitis	.910
Scrofulous diseases of the eye	.039
Iridochoroiditis with meningitis	1.424
Atrophy of optic nerve, cerebral	6.961
Atrophy of optic nerve, spinal	2.333
Atrophy of optic nerve, or neuritis following hematemesis	.396
Atrophy of optic nerve, after vomiting, not blood.	.079
Atrophy from hemorrhage from piles	.039
Atrophy after facial erysipelas	.079
Atrophy with insanity	.039
Atrophy with epilepsy	.158
Atrophy with dysentery	.079
Retinitis nephritica	.198
Diseases of the eye from typhus	.949
Diseases of the eye from measles	.633
Diseases of the eye from scarlatina	.514
Diseases of the eye from variola	2.216
Diseases of the eye from exanthemata (?)	.235
Diseases of the eye from heart disease	.039
Diseases of the eye from childbirth and pregnancy	.431
Intoxication amaurosis	.039
Blindness from disease of the orbit	.039

Congenital anomalies constitute four per cent. of the causes of blindness. The majority of instances occur as a result of consanguineous marriages, or where there is an hereditary tendency toward defects of the eye, or as a result of syphilitic manifestations in intrauterine life. They are usually hopeless—cataract being the only cause in this category which is amenable to treatment. Among thirty-four children, the offspring of fourteen marriages in which one or both parties were blind from birth or childhood, Magnus found eight cases, *i.e.* 23.5 per cent., of blindness or bad sight.

The various ages at which other causes of blindness arise are well shown in Table X. from Magnus, which gives the percentage of causes at the ages when they are developed.

Table X.

Proportion of blindness in 10,000, and the percentage of its causes at different ages.

Cause of blindness.	1 to 5 years.	6 to 10 years.	11 to 15 years.	16 to 20 years.	21 to 25 years.	26 to 30 years.	31 to 40 years.	41 to 50 years.	51 to 60 years.	61 to 70 years.	71 to 80 years.
Ophthalmia neonatorum..	1.99										
Trachoma		0.04						0.07	0.02	0.05	0.12
Injuries.....	.01	.04	0.02	0.05	0.10	0.21	0.13	.19	.05		
Optic-nerve atrophy of all forms . . .	.35	.26	.27	.26	.30	.28	.69	.61	.47	.26	.12
Uveal tract with choroido-retinitis, retinitis pigmentosa .	.27	.11	9.14	.13	.27	.28	.25	.29	.32	.49	.12
Detachment of retina . .	.01	.04	.07	.05	.20	.24	.11	.14	.29	.10	
Glaucoma							.07	.27	.65	1.50	1.30
Operations ..							.01		.05		.25
Corneal diseases.	.27	.04	.04	.02	.13	.14	.05	.04	.14	.10	
Variola ...	.13	.04		.02				.02			
Measles	.13		..								
Scarlatina .. .	.07	.04									
Typhus	.01	.04	.07	.15	.03	.03					

The various causes of blindness, as given in Table IX., will now be considered individually, with such remarks and deductions as are of general interest.

(1) *Ophthalmia neonatorum* furnishes 10.876 per cent. (some statistics place the percentage of blindness from ophthalmia neonatorum as high as twenty-five, but these figures are largely influenced by statistics of orphan asylums where the young only are included) of the blind, a larger proportion than any other single cause—which in itself invests it with grave importance; and this importance is greatly enhanced when it is considered that blindness from this cause means an entire life of blindness; that this disease can be practically prevented by proper prophylactic measures; and further, that even after it is developed, prompt, energetic, and appropriate treatment will usually bring it to a successful termination without impairment of sight. The simple measure of washing the eyes of all infants with warm water as soon as they are born, and instilling a few drops of a two-per-cent. solution of silver nitrate into the conjunctival sac, and subsequent attention to cleanliness, as practiced by Credé, would almost banish this disease from our lists, as has been lately proven in the Maternity Hospital in Vienna and other similar institutions. Ophthalmia neonatorum is almost always caused by the irritating discharges from the vagina, which gain access to the eye either during birth, or, later, by the careless handling of the infant with unwashed hands which have been about the vulva. And it should be borne in mind that these discharges may produce inflammation in any conjunctiva with which they come in contact. Furthermore, the contagiousness of conjunctival discharges should never be overlooked, and this action should always be explained to those who have to deal with any form of conjunctivitis. As a rule, the contagious material from a mild form of conjunctivitis will produce a slight attack in another eye, and *vice versa* for virulent forms. Yet this is not always the case.

(2) *Trachoma and blennorrhea* (purulent conjunctivitis) *of adults*, with a percentage of 9.492, come next. *Trachoma* occurs chiefly in the lower walks of life, where, from necessity or indifference, there are overcrowding, bad ventilation, lack of cleanliness, and a general disregard of the laws of hygiene. It is often seen in the poor and neglected of our city population, in the crowded barracks of military camps, and in the confined quarters of northern latitudes. Its development is favored by low and damp localities on the one hand, and by dry and sandy districts on the other. The contagiousness of the secretion is also an important element in the spread of the disease in crowded quarters. The presence of trachoma, even in a mild form, renders an eye very prone to take on an active form of inflammation (blennorrhea), which will assume epidemic character if conditions favor its spread, as is seen in Egyptian or military ophthalmia. Once developed, trachoma becomes always an obstinate, and often a serious, disease; hence prophylactic measures against it are of the utmost importance, and they are to be found in a correction of the sanitary conditions referred to. Its local treatment should be prompt, energetic, and persistent.

Blennorrhea (purulent conjunctivitis) *of adults* may arise from the same conditions that produce trachoma, and it is often an outgrowth of the latter. It is frequently—in fact usually—the result of contagion of gonorrheal origin. The discharge from any form of conjunctivitis, as also leucorrheal or other irritative discharges, gaining access to the eye may produce the disease. The observance of care and cleanliness with proper regard to hygiene, would cause both of these diseases to disappear, and appropriate treatment would cure most cases, even after the disease had developed.

(3) *Diphtheritic Conjunctivitis.*—Diphtheritic and membranous ophthalmia are sometimes caused by direct infection of the conjunctiva by diphtheritic material from the throat of another person, while in other cases the diphtheritic process creeps up the nasal duct from the nose, and thus reaches the lining membrane of the eye. But in the majority of cases of diphtheritic ophthalmia the disease is a local one, in which the inflammation takes on this special form. No doubt there is often something peculiar in the patient's health, or in the state of his eye tissues,

which gives a proclivity to this particular pathological process. These cases are, for instance, seen with particular frequency after measles, and less commonly during or after scarlet fever, and are more likely to occur in children than in adults. The existence of old, granular disease of the conjunctiva also gives a strong tendency to a diphtheritic type of inflammation, and the same tendency is seen sometimes in a well-marked degree in ophthalmia neonatorum, and in gonorrheal ophthalmia.

(4) *Disease of the Cornea.*—This furnishes rather a large contingent of blind, and it is not to be wondered at when we consider that transparency and regularity of curve of this membrane are essential to good vision. Keratitis, in its various forms, may leave opacity sufficient to cause blindness; and the same is true of superficial ulceration; while deeper ulceration may lead to prolapse of the iris, displacement or obliteration of the pupil, etc., and all are at times liable to be followed by softening of the cornea, with development of staphyloma, etc. Hypopyon keratitis furnishes a larger number of blind than all other corneal affections put together. Keratoconus and keratoglobus are sometimes causes of blindness.

(5) *Iridochoroiditis, Cyclitis, Iritis.*—The different diseases enumerated under this heading are placed together, first, because they often combine; and, second, because the structure involved—the uveal tract—is common to each of the several anatomical parts designated. The term *uveitis* is often and advantageously employed to describe, collectively, inflammations in these parts. *Iritis*, uncomplicated, rarely causes blindness; yet it may do so if the pupil becomes glued down to the lens and the pupillary space becomes blocked with exudation (*occlusion of pupil*). Both this condition and that of *exclusion of pupil* (complete posterior synechiæ) are very apt to be followed by *secondary glaucoma*. More frequently synechiæ from previous inflammation cause recurrent attacks of iritis; and the inflammatory process, extending to the choroid, or to the ciliary body, or to both, gives rise to opacities in the vitreous, and later to detachment of the retina, cataract, etc. The trouble may begin in the choroid, or, less frequently, in the ciliary body, and, extending to other parts or remaining in either locality, may cause blindness in the same way.

(6) *Choroiditis myopica* (6) *and detachment of the retina* (11) will be treated of together under the head of the latter, both being considered as effects of myopia.

(7) *Choroiditis, Retinochoroiditis.*—The choroid and retina are so intimately associated that it is difficult to have an affection of one of these structures without involvement of the other. Syphilis, acquired or inherited, is the usual cause; and blindness is produced by the formation of opacities in the vitreous and disturbance or destruction of the retinal elements.

(8) *Retinitis Pigmentosa, Acquired.*—Though this affection may be developed at almost any period of life, it cannot be considered an acquired disease, for it occurs in particular groups of individuals who, from hereditary tendencies or from consanguineous marriages, show congenital deficiences in this and in other ways. Such cases are hopeless; and even when the disease is recognized in an early stage little or nothing can be accomplished in the way of treatment.

(9) *Retinitis Apoplectica.*—The chief significance of this disease is the index which it furnishes of the condition of the blood-vessels in the brain; for it is usually but a precursor of similar trouble within the cranium.

(10) *Neuroretinitis*, as an idiopathic affection, is almost unknown. It usually occurs as an accompaniment of some other disease—as syphilis, Bright's disease, intracranial disease, pregnancy, cardiac disease, etc.; but as these diseases are specially considered as sources of blindness further on, we are reduced to very narrow limits. It must be admitted that cases of neuroretinitis are occasionally seen without apparent cause. And it is probable that such vague causes as prolonged exposure of the eyes to very bright light, with great heat, as the glare of a furnace, or to the reflection of the sun from the waters of the tropics, or from excessive use of the eyes by strong, artificial light, may produce the disease and thus lead to blindness.

(11) *Detachment of the Retina and* (6) *Choroiditis Myopica.*—Myopia, the cause common to each of these conditions, is of great importance, and merits careful consideration. It may be said to be an outgrowth of civilization and education, and it may be taken as an index of the studious habits and of the close eyework of a people. In this present busy age of progress and competition, which calls for work at high pressure, and necessitates the forcing process as soon as school days are begun, there are many causes at work which serve to swell the ranks of myopes, and to lay the foundation for future increase. The long hours of confinement in the schoolroom, and the lack of proper out-of-door exercise and fresh air, tend to cultivate sedentary habits and to lessen the resisting power of the tissues of the body. The close application of the eyes at near work, with badly constructed desks and insufficient illumination, which necessitate stooping over the pages and straining the eyes, brings on congestion of the fundus of the eye, with thinning and bulging of the sclera at the point of least resistance—the posterior pole; and the development of myopia is the consequence. This condition, once produced, is increased by a continuation of the causes which induced it; and, in unpromising subjects, even the removal of these causes does not put a stop to its progress.

The development and increase of myopia during school life are nowhere better shown than in the following table, taken from Fuchs and prepared by Cohn. The village school corresponds to our lowest grade, and then follow in regular sequence the higher grades, until the last or university course is reached:

TABLE XI.

	Percentage of myopia.	Degree of myopia.
Village school	1.4	1 24.4
Elementary school	6.7	1/22.7
Intermediate school	10.3	1/21.9
High school	19.7	1/19.6
Gymnasium (college)	26.2	1/18.7
University	59.0	1/12.2

It was furthermore noted that the percentage of myopia increased in each school from class to class. Among theological and medical students, whose term of study is prolonged beyond the ordinary university course, the percentage of myopia is still further increased, reaching in the case of theological students seventy-eight per cent. And in reference to confinement and indoor life on the one hand, and out-of-door life and exercise on the other, Erisman found the percentage of myopia in resident scholars to be forty-two per cent., and in day scholars to be thirty-five per cent. Dor found even a greater difference—thirty-three per cent. against eighteen per cent.

Myopia abounds among studious people, and is almost unknown among the ignorant and illiterate. It is not congenital, yet the tendency to its development is certainly transmitted from parent to child. The prophylactic measures against myopia are

of the utmost importance. First and foremost are: A proper amount of out-of-door exercise during school life; well-ventilated schoolrooms, with good illumination, properly constructed desks, so that the light will fall to best advantage upon the page, and avoidance of the habits of stooping or bending the head over the work, and of holding objects close to the eyes. After the development of myopia, much can be done for its relief by the use of atropine and the wearing of properly selected glasses. It should be remembered that myopia fosters sedentary and studious habits; and it at times becomes advisable to discontinue the use of the eyes for near work altogether; and it not infrequently falls within the province of the physician to decide upon the child's future mode of life and employment.

A few cases of myopia with choroiditis occur independently of the causes here ascribed to it; yet they are so infrequent that they may be left out of consideration. And, too, detachment of the retina is sometimes seen in eyes that are not myopic; but it rarely occurs in such as a primary affection, and when secondary to some other pathological lesion, that, and not the detachment, is the cause of blindness.

(12) *Glaucoma.*—The importance of this disease, as indicated by its quota of blind, is forcibly increased, when its usual amenability to treatment is considered. While a well-marked case of glaucoma presents unmistakable symptoms of the disease, which it would be unpardonable to overlook, there are other cases which are obscure and misleading. The very fact of this uncertainty should, however, put us upon our guard; and there are few cases indeed which would run the gauntlet of careful examination and close observation. Once recognized, prompt and energetic treatment is indicated; and there is no operation in the whole range of surgery that affords more brilliant results than does iridectomy in cases of acute glaucoma. Sclerotomy and eserine have their spheres of usefulness; and stretching the external nasal nerve has recently been much lauded in the treatment of certain obstinate forms of glaucoma. Unfortunately the more obscure cases attract but little attention until the disease is far advanced, and medical advice is sought only after serious and permanent impairment of sight comes on. A more thorough knowledge of the disease and greater familiarity with its symptoms by the general practitioner will not only insure its more prompt recognition, but will lead the laity to a better understanding of the affection, and cause greater care in the observance of eye symptoms. A few cases of glaucoma are strongly allied to optic-nerve atrophy, and these are very unfavorable.

(13) *Idiopathic optic-nerve atrophy* occurs most frequently in subjects who have inherited a tendency to nervous disorders. It is often a precursor of spinal cord or of cerebral disease; and as the length of time which may intervene between the development of optic atrophy and central changes is often considerable, the diagnosis is usually difficult and uncertain. The disease is one of the most obscure that we have to deal with, and the prognosis is unfavorable. It is much more frequent in men than in women.

(14) *Tumors of the Eye and its Surroundings.*—*Malignant diseases*, as glioma of the retina, sarcoma of the choroid, of the ciliary body, and of the iris, and epithelioma or lupus of the conjunctiva, or of the cornea, may produce blindness through destruction of the globe by their own growth; yet their chief importance is in their danger to life. Cysts of the iris, if they are not removed, may cause blindness by increase in size. *Gummata* of the ciliary body and of the sclera may also produce blindness in the same way. Other tumors of the eye rarely cause blindness. Tumors arising from parts adjacent to the eye may produce blindness, directly by extension of the disease to the globe, or indirectly by pressure effects upon the globe or optic nerve, as is seen in vascular and cystic tumors of the orbit, and in tumor or distention of the frontal, ethmoidal, nasal, or maxillary sinuses.

(15) *Unclassifiable.*—The percentage here given may be taken as a fair example of the proportion of the blind which present such complicated conditions as to preclude classification.

(16) *Direct Injury of the Eyes.*—The more important proportion of these cases occur in individuals whose labor necessitates exposure of the eyes to flying bits of metal or stone, as machinists, workers in stone, miners, etc., and in those who have to deal with explosives, as in blasting, the manufacture of explosive materials, etc. The use of protective glasses, preferably of mica, which combines perfect transparency with considerable strength, is a measure that would afford much protection to the eyes, though it has been but little adopted by workmen exposed to these dangers.

A certain number of cases occur from unavoidable and unforeseen accidents, and of these it is unnecessary to treat.

Injuries of the eye in the German army during the Franco-German war (1870-71) were met with in 786 cases—being 0.79 per cent. of the whole number of injuries , and 7.8 per cent. of head injuries; and affections of vision after head injuries were met with in 74 cases—or 0.7 per cent. of head injuries.

(17) *Unsuccessful Operations.*—The percentage here furnished certainly appears small, when it is considered that many eye operations are attended with considerable risk to the eye, even in the hands of the most accomplished operators. Cataract extraction—the most important operation in ocular surgery, and at the same time the most formidable—is accountable for most cases of blindness from operative measures. As it is performed late in life, when the process of repair is impaired by age and often by disease, it is to be wondered that the proportion of unfavorable results is not larger.

(18) *Injuries of the head* produce blindness through lesions of the optic nerve, at or about the optic foramen. It is known that blows upon the head may cause fracture of the bones about the apex of the orbit, or at the optic foramen; and blindness ensues from injury to the optic nerve—immediately if the injury be severe, and more slowly if dependent upon secondary degenerative changes (atrophy). Meningitis following injuries of the head may cause optic neuritis or atrophy and blindness. And injuries of the angular gyrus may produce blindness.

(19) *Traumatic Sympathetic Ophthalmia.*—This is one of the most important of eye diseases, and, because of its insidious character and its intractable and uncertain course, merits the utmost care in its consideration at the hands of ophthalmologists, and general practitioners as well. Resulting, as it does, from previous mechanical injury which has greatly impaired or entirely destroyed the fellow eye, its treatment involves great responsibility. And as it not infrequently happens that the sympathizing eye is ultimately left in a worse condition than the exciting one, advice should be well and intelligently considered. The disease may appear within a few weeks, or it may not develop for years; and while its prodromes may extend over periods varying from weeks to months, it sometimes comes on unannounced, and quickly leads to blindness. Arising at times from wounds, apparently trivial, in the ciliary region, it occasionally fails to appear after extensive injury to this, the vulnerable zone. Treatment of the disease after it has developed is of course important, and while it is sometimes unsatisfactory, it is usually productive of great good. The measure above all others to be adopted is prophy-

laxis; and this includes the proper care of the primarily injured eye, as well at the time of the injury as later on; and this of course involves the question of enucleation. This is an important problem, and there are many points to be carefully considered before a conclusion is reached. It may be stated as a cardinal point, however, that an eye so seriously injured in the ciliary region as to preclude the possibility of retention of sight should be promptly removed; for such an eye is not only a useless organ, but is a source of constant menace to its fellow.

(20) *Diseases of the Eye from Syphilis.*—Syphilis is a prolific source of eye disease, and may cause almost any form of it. The *inherited* form of syphilis, through defective development or inflammation of the several parts of the eye during intrauterine life, may cause blindness. And abnormalities in the osseous development of the orbit or of the skull may, through pressure upon the visual tract, cause optic neuritis or atrophy and blindness. Diffuse (parenchymatous) keratitis—a disease of early life—is also occasionally productive of blindness. Either the *inherited* or the *acquired* form of syphilis may cause blindness through keratoiritis, iritis, iridocyclitis, iridochoroiditis, choroiditis, retinochoroiditis, and optic neuritis or atrophy. In tertiary syphilis, gummata—affecting by preference the sclera or the ciliary body—may produce destruction of the eye. And the periosteal or bony lesions of this stage may cause, through participation or by their pressure effects, disease of the eye or of its conducting apparatus, which leads to blindness. An early recognition of the specific taint, and prompt and energetic measures against it, constitute the sheet-anchor of success in all diseases dependent thereon.

(21) *Gonorrheal Conjunctivitis.*—This is a most virulent form of purulent ophthalmia, due to inoculation of the conjunctiva with the discharge from a specific urethritis or vaginitis. The material is conveyed to the eye by accident or by carelessness, through unwashed hands in persons with gonorrhea, or in those treating it, and the use of towels or of linen which have become contaminated. Perfect cleanliness and care, observed by gonorrheal subjects and by their attendants and associates, would expel this disease from the category of eye affections.

(22) *Scrofulous Diseases of the Eye.*—The strumous condition is a fruitful source of eye disease, yet the diseases to which it most frequently gives rise—ophthalmia tarsi, phlyctenular troubles, etc.—seldom cause blindness. One of its diseases, however—cyclokeratitis—is a most serious disease, and often produces blindness. It was first described by Dalrymple, and is sometimes spoken of as Dalrymple's disease. It is fortunately rare. Lupus is usually considered a strumous disease, and this may lead to destruction of the eye—whether attacking the eye primarily, or involving it secondarily. Tuberculosis may also cause blindness, through choroiditis, iritis, and keratitis.

(23) *Iridochoroiditis with Meningitis.*—This disease is commonly spoken of as metastatic choroiditis, and is caused by an extension of inflammation from the head to the eye in simple meningitis, or, as is more frequently seen in cerebrospinal meningitis, by metastasis. The disease usually destroys the eye, and treatment is ordinarily unavailing.

(24 and 25) *Atrophy of the Optic Nerve (Cerebral and Spinal).*—It is often difficult and sometimes impossible to locate the lesion upon which optic-nerve atrophy depends, and it will be convenient to consider these two forms together. According to Galezowski, who tabulated 166 cases of optic-nerve atrophy, about 50 per cent. are due to diseases of the brain and spinal cord; 13 per cent. are traumatic; 9 per cent. are due to alcoholism; 8 per cent. to syphilis, and the remaining causes are of the most varied kind. And according to von Graefe, about 30 per cent. of cases of primary atrophy of the optic nerve are due to spinal disease.

Cerebral optic-nerve atrophy may be consecutive to optic neuritis (of central origin), or it may follow lesion of the chiasm, of the cerebral centers, or of the cortex about the angular gyrus, or it may be caused through pressure upon the nerve by an exostosis, tumor, or aneurysm; through narrowing of the optic foramen by hyperostosis or by pressure upon the chiasm from distention of the third ventricle. Meningitis, chronic or acute, may also cause ptosis, or atrophy without recognized neuritis, etc. *Spinal atrophy* occurs with locomotor ataxia, of which it may be the earliest symptom; or it may, as is often the case, come as a late manifestation of the disease.

(26) *Atrophy of the Optic Nerve, or Neuritis after Hematemesis.*—Loss of blood is occasionally followed by affection of vision, which may be temporary or permanent. It is with the latter that we have to deal, and this usually depends upon either neuritis or atrophy. Clinical experience has taught that hemorrhages from the gastrointestinal tract cause disturbance of vision more frequently than hemorrhages from other localities (thirty-five per cent.). The connection between the loss of blood and disease of the optic nerve has so far received no satisfactory solution. The same connection probably exists between *atrophy of the optic nerve after bleeding from piles* (27), and *after dysentery* (28).

(29) *Atrophy of the optic nerve after vomiting* is rare, and the connection between the two is obscure. The straining and consequent congestion may produce retro-ocular hemorrhage, or serous effusion; or it may be due to the connection which exists between the stomach and the corpora quadrigemina.

(30) *Optic-nerve atrophy after facial erysipelas* is usually caused by an extension of the cellulitis to the tissue of the orbit, and the resulting damage to the trunk of the nerve.

(31) *Atrophy of the Optic Nerve with Insanity.*—Atrophy sometimes occurs among the insane, and most frequently in subjects of general paresis—though it may occur in dementia and in other forms of insanity. It is a degenerative change, associated with similar lesions in the central nervous system.

(32) *Atrophy with Epilepsy.*—It does not appear that idiopathic epilepsy has connection with any form of eye disease. It is only in such cases as are dependent upon gross intracranial lesions that changes are observed in the disc, and the atrophic changes here differ in no way from those seen in the usual forms of brain disease.

(33) *Retinitis nephritica* occurs in about twenty-five per cent. of cases of chronic Bright's disease. It is more important as a means of diagnosis than as a cause of blindness, for not infrequently it is the first symptom which leads to a detection of disease of the kidney. It rarely causes blindness, however, in spite of the marked pathological changes that are noticeable in the retina, and often in the optic nerve.

(34) *Diseases of the Eye with Typhoid.*—Loss of sight has been many times observed during convalescence from typhoid fever, and, subsequently, optic-nerve atrophy has usually been found. In some of these cases cerebral symptoms have been observed, and in others there was none. Keratitis is sometimes seen, and blindness may be one of its consequences.

(35) *Blindness from measles* may be due to optic neuritis, or it may result from neglected diseases of the external eye, *i.e.* conjunctivitis, keratitis, etc.

(36) *Disease of the Eye from Scarlatina.*—The frequency with which renal disease accompanies scarlet fever renders affections of sight not very rare consequences of the disease. Yet neuroretinitis does occur without the presence of renal disorder. Atrophy of the optic nerve may also be the result of scarlatina. In malignant cases sloughing of the cornea has been observed, and in other cases keratitis may produce blindness.

(37) *Disease of the Eye from Variola.*—Variola may cause neuroretinitis or atrophy of the optic nerve;

but its chief danger is from diseases of the external eye, almost any part of which may be the seat of the eruption. The most dangerous seat is the cornea, where ulceration often leads to blindness. Iritis has also been observed. Important as the local treatment of these disorders may be, the prophylactic measure of vaccination should supersede them all, and thus prevent entirely the disease upon which they depend.

and the small proportion embraced under the *last*. Absolute accuracy in this arrangement is, of course, not claimed, but it will serve the purpose of illustrating the large amount of blindness arising from avoidable causes, and such as are amenable to treatment.

There are certain *irregular forms of blindness* which will be treated of under appropriate headings elsewhere and it will be necessary to refer to them here only in a general way. The free exhibition of *qui-*

TABLE XII.

Preventable causes of blindness.	Per cent.	Probably preventable blindness.	Per cent.	Unpreventable blindness.	Per cent.
Ophthalmia neonatorum	10.876	Diseases of the cornea	4.034	Diseases of the cornea	1.034
Trachoma and blennorrhea	9.492	Direct injuries of the eye	2.017	Direct injuries of the eye	2.017
Diphtheritic conjunctivitis	.356	Unsuccessful operations	1.978	Tumors of eye and surroundings	.356
Choroiditis myopica	.949	Iridochoroiditis, cyclitis, iritis	4.430	Iridochoroiditis, cyclitis, iritis	4.430
Detachment of retina	3.746	Detachment of retina	1.000	Injuries to the head	.277
Glaucoma	8.000	Glaucoma	.978	Scrofulous diseases	.039
Sympathetic ophthalmia	4.509	Unclassifiable	1.681	Unclassifiable	1.681
Gonorrheal ophthalmia	.910	Diseases of the eye from syphilis	.238	Disease of the eye from syphilis	.238
Diseases of eye from smallpox	2.216	Choroiditis, chorioretinitis	.369	Choroiditis, chorioretinitis	.738
Intoxication amaurosis	.039	Idiopathic optic-nerve atrophy	2.000	Idiopathic optic-nerve atrophy	5.751
		Optic-nerve atrophy, cerebral	2.000	Optic-nerve atrophy, cerebral	4.961
		Optic-nerve atrophy, spinal	.333	Optic-nerve atrophy, spinal	2.000
		Typhoid, measles, scarlatina, etc.	1.165	Typhoid, measles, etc	1.165
				Iridochoroiditis with meningitis	1.424
				Other causes, including 3.835 per cent. of congenital blindness	5.412
	41.093		22.223		34.523

38) *Disease of the Eye from Heart Trouble.*—The most frequent cause of blindness from heart disease (valvular) is the so-called embolism of the central artery of the retina. This is usually monocular, but sometimes both eyes are affected. Thrombosis of the central vein of the retina behind the eye, in association with disease of the heart, may also produce blindness. In ulcerative endocarditis retinal hemorrhages often occur, and sometimes panophthalmitis is observed.

(39) *Diseases of the Eye from Childbirth or Pregnancy.*—In pregnancy we are liable to have albuminuric retinitis, and, following childbirth, we may have metastatic choroiditis, or retinal hemorrhage; and cases of atrophy of the optic nerve are sometimes dependent upon lactation.

(40) *Intoxication Amaurosis.*—Under this head are included cases of blindness resulting from the abuse of certain noxious agents, chief among which are alcohol and tobacco. It is claimed that the free and long-continued use of either of these substances not infrequently leads to a form of optic-nerve atrophy possessed of certain distinctive peculiarities. There seems to be good reason for attributing such to alcohol, but the reasons in favor of tobacco are not so strong.

(41) *Blindness from Diseases of the Orbit.*—Inflammatory processes in the orbit, whether in the cellular tissue or in the periosteum or bone, may cause either simple atrophy of the optic nerve or neuritis and consecutive atrophy. With much swelling of the orbital tissue there is danger that the nutritive supply of the globe may be cut off by pressure, and that the inflammation or sloughing which results may produce blindness. Tumors of the orbit may act as inflammatory products, or, the disease extending to the eye, may directly cause destruction of this organ.

An important matter in the consideration of the causes of blindness, is the proportion composed of those whose origin is unavoidable, and the course of which is beyond control. If arranged under the headings of *Preventable, Probably Preventable,* and *Unpreventable Blindness,* we are at once struck with the large number included under the *first* and *second* headings,

nine or of *salicylic acid* sometimes causes blindness, and it has been observed in rare instances to follow the use of *silver,* of *mercury,* and of *lead.* Prolonged exposure to the fumes of *sulphide of carbon* may produce amblyopia; and the fumes of *osmic acid* may bring about the same condition. The circulation, in the blood, of a superabundance of *urea* is apt to cause transient attacks of blindness. And in *migraine,* or sick headache, attacks of blindness are not infrequent. The attacks of blindness in the foregoing conditions of the system are usually transient, and perfect recovery quickly follows: yet, if they are often repeated, permanent impairment of sight may result, which in some instances declares itself as a low grade of optic neuritis or atrophy. *Hysterical amblyopia* is a recognized condition. It is temporary and irregular, and is usually attended by other hysterical symptoms. Temporary blindness may occur as the *aura* of an *epileptic attack.* Cases of *word-blindness* which were dependent upon lesions about the angular gyrus have been observed in individuals who could talk and even write. *Night-blindness* or nyctalopia is a condition of torpor of the retina which usually affects those who have been long exposed to bright lights—as sailors or marching soldiers, in the tropics. Insufficient food, either as to quantity or quality, seems also to be a factor in the disease. *Day-blindness,* or *hemeralopia,* is a form of retinal hyperesthesia which is also usually caused by long exposure to glistening surfaces brilliantly illuminated by the sun. *Snow* or *ice blindness* is a variety of hemeralopia, though there are usually with this form signs of conjunctival implication. *One-sided blindness,* or *hemianopsia,* which may exist in various forms, is occasionally seen, and it is often of importance in locating intracranial lesions. *Blindness from disuse—amblyopia ex anopsia*—is claimed by many to result from the long-continued disuse of an eye. *Simulated blindness* can usually be detected, yet it is often done with difficulty. *Color-blindness—achromatopsia*—may exist in various forms. It is of great importance, and receives ample consideration elsewhere.

Asylums for the Blind.—It may be of interest to state that the first institution for the blind was founded in Memingen, by Weef VI., in 1178: the second in Paris, by St. Louis, in 1260; the first for the employment of adult blind was opened in Edinburgh, by Dr. Johnston, in 1793. There were, in 1873, 148 institutions for the blind in the world; and their number has greatly increased since that date.

The number of the blind gainfully employed in this country, according to the U. S. Census Reports, 1900, was 12, 506, distributed as follows:

	Per cent.
Agricultural pursuits...	12.2
Professional service...	11.2
Domestic and personal service...	14.2
Trade and transportation...	13.4
Manufacturing and mechanical pursuits...	19.0

Prevention of Blindness.—Much can be done toward preventing blindness through a better understanding of its causes by the laity, while the profession should not only be alive to these points, but should be able quickly to recognize diseases of the eye, and acquanted certainly with the simpler forms of treatment. The most prolific source of blindness—ophthalmia neonatorum—can be stamped out by the observance of the simplest procedure—Credé's method—already referred to. So important is this disease that the legislatures of some of the European countries, and of some States in our Union, have enacted laws for the guidance of those concerned.

The act of New York, which will serve as an illustration, is given here:

"An Act to Prevent Blindness.

"Sect. 1. Should any midwife or nurse having charge of an infant in this State notice that one or both eyes of such infant are inflamed or reddened at any time within two weeks after its birth, it shall be the duty of such midwife or nurse, so having charge of such infant, to report the fact in writing within six hours to the health officer, or some legally qualified practitioner of medicine of the city, town, or district in which the parents of the infant reside.

"Sect. 2. Any failure to comply with the provisions of this act shall be punishable by a fine not to exceed one hundred dollars, or imprisonment not to exceed six months, or both.

"Sect. 3. This act shall take effect on the first of September, 1890."

James Lancelot Minor.

Blisters.—See *Counterirritation*.

Block Island.—This island (lat. 41° 13′ N., long. 71° 35′ W.), situated about midway between Pt. Judith on the Rhode Island coast and Montauk Point, lies about fifteen miles off the coast, and is far enough out to sea to afford a purely marine climate. In this respect it is comparable with Nantucket, the Isles of Shoals off the New Hampshire coast, and Monhegan off the Maine coast.

The island is a small one, seven or eight miles long from North to South, and from two to five miles wide. The greater part of the island is considerably elevated above the sea-level, and consists of an undulating, uneven surface with hills and valleys. The rocky bluffs lying upon the Southern and Southeastern shores are said to rise some 200 feet above the water, rendering this part of the coast exceedingly picturesque and bold in appearance.

On the Eastern shore where the principal hotels are located there is a good beach for bathing. There are also excellent facilities for boating and fishing.

From its situation out at sea, with the wind coming from the ocean, from whatever direction it blows, one experiences the same conditions of climate as at sea on shipboard without the discomfort of sea-life and the possibility of sea-sickness. Situated at this particular locality in the Atlantic Ocean, the air is cool, pure, invigorating and at the same time soothing. The humidity, of course, is high, as with all sea climates.

Such climatic characteristics are favorable for cases of neurasthenia and those suffering from temporary depressed vitality from whatever cause. Cachectic conditions and children with bone and glandular tuberculosis should do well here; also cases of malarial poisoning. Insomnia may or may not be benefited by sea-air; a trial only can determine.

There are many hotels on the island of various degrees of excellence, and cottages said to be especially adapted for invalids and convalescents.

The island is reached from New York, Providence, Newport, and New London.

There is a station of the U. S. Weather Bureau here, and the following climatic data are from the official observations.

Meteorological Data of Block Island for the Four Months, June, July, August, September, from 1890 to 1897, Inclusive. Fahrenheit Scale.

Year.	Mean average temperature for the 4 months.	Mean maximum temperature.	Mean minimum temperature.	Relative humidity.
	degrees	degrees	degrees	per cent.
1890....	65.2	73.0	60.0	87.3
1891....	65.2	81.0	52.7	89.0
1892....	65.7	81.0	53.0	86.4
1893....	64.4	79.7	51.5	85.0
1894....	65.9	80.5	52.5	85.5
1895....	65.8	81.5	50.0	86.6
1896....	65.5	80.0	52.5	86.5
1897....	65.4	79.9	51.7	85.7

The mean average temperature of the summer proper is 67° F.; of autumn, 53° F.; winter, 32° F.; spring, 43° F.; and the annual mean is 56° F. The mean annual rainfall is 53 inches. Sunshine for summer, 63 per cent.; autumn, 43 per cent.; winter, 51 per cent.; and spring, 48 per cent.; annual mean, 53 per cent. (*Medical Record*, 1897.)

In a private letter received from a gentleman who has passed many summers on the island, the following is extracted: "There is more or less fog on the island, but generally not enough to be uncomfortable; the bathing is good and perfectly safe. There is almost always a breeze, and, of course, no land breeze, so that the weather is cool and comfortable and no one need fear any discomfort from the heat; there is practically absolute freedom from mosquitos."

Edward O. Otis.

Blood.—Although frequently referred to as the nutritive fluid of the body, from the standpoint of modern histology and physiology, blood is more properly considered as a tissue, the intercellular substance of which is fluid. Compared with other body tissues, it is more unstable, both its physical and chemical properties being affected by a greater number of influences. It contains a greater variety of morphologically and functionally dissimilar constituents than do other tissues, and because of the fluid nature of its intercellular substance, the definite and fixed relationship between cells and matrix is not present as in other tissues. It is kept in constant motion by the muscular action of the heart, and is present in all body structures, but does not normally receive formed elements from them. It does, on the other hand, by means of diapedesis, give up its cells to other tissues.

Properties.—Blood is composed of the *plasma*, or liquor sanguinis, the fluid portion, and innumerable microscopic bodies, the *corpuscles*, held in suspension. The latter consist of two distinct varieties—the *erythrocytes*, or red corpuscles, and the *leucocytes*, or white corpuscles. Besides these, and classified with them as corpuscular elements, are the *thrombocytes*, sometimes called platelets or plaques, and *hemoconia*, or blood-dust. At present we are probably not justified in calling these true cell elements, but should adhere to the belief that they are simply transformation products of better known cells.

Color.—In thin films, blood appears by transmitted light, as do the individual red corpuscles, to be of a greenish-yellow or straw color. To the naked eye, even in thin layers, it is opaque. The red color which one mentally associates with blood, is not due to the plasma, but is an optical effect produced by the superimposed layers of hemoglobin-filled red corpuscles. It is only in mass that blood is red. Variations in color, then, are dependent upon the mass of blood under observation, upon the red cell content, upon the hemoglobin index, and upon the relative amounts of oxygen and carbon dioxide contained. Of these factors, the last is probably of the most importance. The blood of the pulmonary vein, in that it contains relatively less carbon dioxide and more oxygen than elsewhere, is of a bright red color, while that of the pulmonary artery, which is rich in carbon dioxide, and poor in oxygen is dichroic, that is, bluish-purple by reflected, and greenish by transmitted light. The administration of various drugs and toxic gases provokes marked color changes, either by altering one or more of the above mentioned factors, or by the formation of distinctly new chemical substances within the blood.

Specific Gravity.—The average specific gravity of the blood at birth is about 1.066. A gradual decline then ensues, until at the third year it is about 1.051. This fall is followed by a slow rise until puberty, when it is about 1.059 in the male (seventeenth year) and about 1.056 in the female (fourteenth year). It remains close to these figures throughout middle life in males, but falls slightly in females. Specific gravity is chiefly dependent upon the hemoglobin, red cell, and fluid content of the blood, which accounts for the differences in age and sex. The specific gravity of the plasma is usually between 1.026 and 1.032, that of the red corpuscles, 1.088 to 1.105, while that of the leucocytes is somewhat lower, as is shown by the fact that when blood clots slowly, as it does normally in some animals, the leucocytes form the upper, and the erythrocytes the lower part of the clot.

Among other causes of variations may be mentioned—thirst, starvation, sleep, exercise, profuse sweating, vasomotor contraction of vessels, acute loss of water through the intestines and kidneys, all of which raise the specific gravity, and drinking of large amounts of water, loss of blood, anemia, chlorosis, and nephritis, which lower it. The reasons for these changes are obvious.

Hammerschlag's method of determining the specific gravity of blood, while not as accurate as some means which have been devised, has the advantage of requiring only a few drops of the blood to be tested. It consists of placing small drops of the blood in a mixture of chloroform (sp. gr. 1.526) and benzol (sp. gr. 0.889), which is mixed in varying proportions to form a series in which the specific gravities are known. The specific gravity of the mixture in which the drop hangs suspended, is the specific gravity of the blood.

The specific gravity of blood is in itself not important, except that it gives us an indication of the hemoglobin. As this is more accurately determined by the hemoglobinometer, the determination of specific gravity is usually omitted from routine blood examinations.

The following table, compiled by Hammerschlag, shows the approximate relation between specific gravity and hemoglobin content:

Specific gravity.	Hemoglobin content, per cent.
1.033 to 1.035	25 to 30
1.035 to 1.038	30 to 35
1.038 to 1.040	35 to 40
1.040 to 1.045	40 to 45
1.045 to 1.048	45 to 55
1.048 to 1.050	55 to 65
1.050 to 1.053	65 to 70
1.053 to 1.055	70 to 75
1.055 to 1.057	75 to 80
1.057 to 1.060	80 to 95

Reaction.—The chemical reaction of blood is always alkaline, because of the presence of disodium phosphate and sodium carbonate. A portion of these substances is combined with the proteins of the plasma, and the remainder is present chiefly in the red corpuscles, in the form of diffusible salts. In testing the reaction of the blood, litmoid, and not ordinary litmus paper, should be used. The degree of alkalinity is expressed in terms of the number of milligrams of sodium hydrate to be neutralized in 100 c.c. of the blood, and varies between 180 and 216. A $\frac{N}{75}$ solution of tartaric acid is usually employed for purposes of estimation, 1,000 c.c. of the solution being required to neutralize 530 milligrams of sodium hydrate. The alkalinity of whole blood is greater than that of the serum, and is increased by an increase in the number of red corpuscles.

The alkalinity is decreased by active muscular exercise, because of the development of lactic acid in the muscular tissue; by the prolonged use of soda; by saturation with carbon dioxide; in fevers and other infections, anemias, diabetes, uremia, scurvy, and cancer. It is less during digestion than when fasting; less in women and children than in men; in nursing women it is less than in pregnant women; and it is decreased by coagulation, old clots being frequently slightly acid. An increased alkalinity is said to increase the immunity of the tissues against bacterial invasion.

Viscosity.—During the past few years, considerable attention has been paid to this property of the blood, for it seems that the degree of viscosity must have some effect upon the circulation as a whole. It is dependent upon the number of red corpuscles present for the most part, and to a lesser degree upon volume changes in the corpuscles, and the carbon dioxide content. It is greatest in polycythemia, and least in the severer forms of anemia. The lessened tendency of the red cells to form rouleaux in the anemias is an evidence of decreased viscosity.

The viscosity of the blood of a healthy individual has been estimated as being about five times that of distilled water at 37° C.

Quantity.—The quantity of blood varies somewhat in different animals and in different conditions of the body. In general, however, it has been estimated at about one-thirteenth to one-twelfth of the body weight in mice, one-twenty-second to one-seventeenth in guinea-pigs, one-twenty-second to one-fifteenth in rabbits, one-eighteenth to one-eleventh in dogs, one-thirteenth to one-tenth in birds, one-twentieth to one-fifteenth in frogs, one-ninteenth to one-fourteenth in fish, in adult humans one-fourteenth to one-thirteenth, and in infants, about one-nineteenth. Thus, an individual weighing 150 pounds would have 4.85 to 4.93 kilograms or 4.58 to 4.65 liters of blood. An average infant at birth (seven and one-half pounds) would contain about 179 grams, or in the neighborhood of 167 c.c. Fat individuals have relatively less blood than lean ones. In starving persons, it may be proportionately greater than in the well-fed, for the reason that in inanition the weight

of the body decreases more quickly than the weight of the blood.

Numerous methods for the determination of the total quantity of blood in the body have been described, but the one which has given the most constant results, and at the same time is relatively convenient, is that of Haldane and Lorrain Smith. A definite quantity of carbon monoxide gas is inhaled by the patient, and the percentage of saturation is estimated by comparing the color of the blood with that of a sample of ox blood of known saturation. From this it can easily be determined how much gas would be required to completely saturate it. As the blood is known to be able to absorb 18.5 per cent. of its volume in gas, the total volume of the blood may thus be readily estimated.

Distribution.—According to Ranke, the liver and skeletal muscles each contain a trifle more than a fourth, the lungs, heart, and great vessels together, a little less than a fourth, and the rest of the body about a fifth of the total blood of the body. The kidney and spleen each contain about one-eighth of their weight of blood, the muscles about one-twentieth, and the liver between one-third and one-fourth of its weight.

It should be remembered, however, that the amount of blood contained in a given part is continually changing, according to its activity. During muscular exercise, for example, the intricate vasomotor mechanism brings about a widening of the small arteries in the muscles, and a corresponding narrowing of vessels in other parts of the body, that the muscles may have an increased blood supply without interfering with the actual blood pressure. The veins of the omentum seem to play a very important part in this reciprocal action, being markedly constricted during processes which call for a large supply of blood in other portions of the body.

Taste.—The blood possesses a saline taste, derived from the salts dissolved in the plasma. Of these, sodium chloride is the most abundant.

Odor.—Blood has a peculiar odor, which differs in the various animal species. The difference is said to be due to varying quantities of excretory products and to the different amounts of the volatile fatty acids which are combined with the alkali of the blood in the various animals. By adding sulphuric acid to a sample of fresh blood, these acids are set free from their combinations, and the characteristic odor becomes more distinct.

Freezing-point.—Blood freezes at about −0.56° C. The freezing-point increases as the oxygen content diminishes, and is dependent somewhat upon the concentration of the salts. In other words, the greater the concentration of the salts of blood, the lower the freezing-point.

Temperature.—The temperature of the blood of the higher animals is practically constant, varying in man from 36.6° to 37.8° C. (97.9° to 100° F.). In the dog it is somewhat higher, averaging 37.9° to 39°, in the mouse, 37° to 38°, and in fowl 40.9° to 44.1°. In the lower forms, such as the frog, it follows closely the temperature of its environment, but never getting far above it. Thus the temperature of the blood of the frog may be 5° C. in January and 30° to 40° in July.

The factors determining the slight variations in blood temperature in the higher animals are numerous, but they all fall naturally under one of two headings —those that influence the rate of heat production, and those influencing the rate of heat loss. Blood temperature varies in different parts of the body, and in the arteries and veins. The general rule, not without exceptions, however, is that of the superficial vessels, the veins carry the coolest blood, while the internal veins carry warmer blood than the corresponding arteries. The warmest blood in the body is found in the portal and hepatic veins, where the temperature changes in direct proportion to the activity of the digestive organs.

Morphology.—The *erythrocytes*, or red blood corpuscles vary in many respects in different animal groups. In amphibians, reptiles, birds, and fish, with the exception of Cyclostomata, they are biconvex ellipsoids containing nuclei. The erythrocytes of man and all mammalia aside from the Camelidæ group, are thin, flattened, biconcave, circular discs, or, according

Fig. 680.—A, Effect of Hypertonic Salt Solution on Red Blood Corpuscles of Man; B, Effect of Acetic Acid; C, Effect of Tannin; D, Effect of Boric Acid.

to some observers, bell-shaped or spherical, but without nuclei. In the Camelidæ, although non-nucleated, they are ellipsoidal in shape.

The fact that the red corpuscles of the fetus in mammals normally contain nuclei and that these nuclei disappear at about the time of birth, has given rise to much discussion among histologists as to whether or not the adult red corpuscles should be termed true cells. It has been repeatedly suggested that the nucleus persists in a finely divided state, and

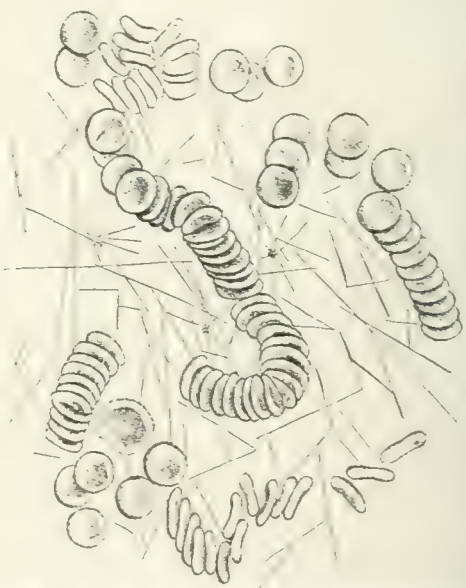


Fig. 681.—Normal Blood; Showing Rouleaux Formation and Fibrin Network. (Da Costa's Clinical Hematology, P. Blakiston's Son & Co., 1905.)

this view is substantiated by the fact that nuclein can be demonstrated in considerable quantities in combination with the hemoglobin. If they are true cells, they must be regarded as a very highly specialized variety, in that they have lost one of the most basal functions of protoplasm, namely, that of reproduction.

As regards the *structure* of the erythrocytes, the most probable view is that they are composed of a spongy and elastic structureless framework, or stroma,

containing from thirty-two to forty per cent. of hemoglobin, or coloring matter. The stroma appears to be protein in nature, and is continuous throughout the mass of the cell. It is, however, denser at the surface than at the center, constituting a physiological envelope which allows the passage of certain substances into or out of the corpuscle, and hinders

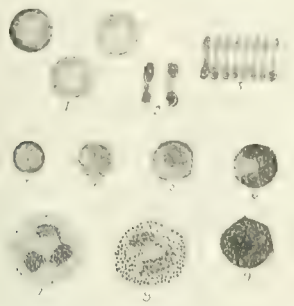


Fig. 682.—Cells from Human Blood. × 600. (After F. R. Bailey.) 1, Red blood cell seen on flat; 2, red blood cell seen on edge; 3, red blood cells forming rouleaux; 4, 4, small and large lymphocytes; 5, mononuclear leucocytes; 6, transitional leucocyte; 7, polymorphonuclear leucocyte; 8, polynuclear leucocyte, containing eosinophilic granulation; 9, mononuclear leucocyte containing basophile granules.

the passage of others. The character of the stroma is doubtless the basis of the extreme flexibility of the red corpuscles, which allows them to accommodate themselves to the smallest capillaries. Combined with changes due to osmotic pressure this flexibility often produces such marked changes in their shape that but few of the typical biconcave discs can be demonstrated in a stained specimen of blood. In such instances we cannot help but agree with those observers who say that the red corpuscles of mammals do, occasionally at least, present the bell-shaped or spherical forms.

In the biconcavity of mammalian red corpuscles we see a repetition of the economic principle so universal in higher animal bodies, namely, the exposure of a maximal surface for diffusion and absorption, with the minimum use of material, the material in this case being the hemoglobin. It has been estimated that the sum of the surfaces of all of the red corpuscles in the body of a man weighing 150 pounds is in the neighborhood of 2,900 square meters, or about 0.716 acre, while the hemoglobin content of his blood is only about 680 grams.

The red corpuscles constitute between thirty-eight and forty-two per cent. of the total weight of the blood in human beings. At birth their *number* in one cubic millimeter of blood ranges between seven and eight million. During the first seven or eight days a rapid decline takes place, the number at the end of this time being between five and six million. From that time until the fourteenth year, the count is about the same in both sexes and bears a close relation to changes in the specific gravity. From the beginning of the female child's menstrual life, however, the red corpuscles number about ten per cent. less than in males, so that throughout middle life the red count is about 4,500,000 per cubic millimeter in females, and about 5,000,000 in males. On this basis, the average man of 150 pounds would have in his 4.6 liters of blood about 23,000,000,000,000 red corpuscles. The above figures are the average at the sea level, but it is not unusual to find the number as much as twenty per cent. higher in healthy individuals.

Removal of a mammal to a high altitude is always followed in a short time by an increase in the count of the red corpuscles, but whether this increase is real or only proportional, that is, whether there is an actual increased proliferation of erythrocytes or whether they become more concentrated owing to removal of water from the plasma, is a disputed point. In either case, the phenomenon is doubtless a provision of nature to compensate for the rarity of the oxygen, and we must suppose that this same rarity of oxygen operates as the necessary stimulus to set the compensatory process in motion.

Outside of the pathological conditions such as severe hemorrhage, various types of anemia, surgical shock, malaria, etc., in which the diminution in number may be extreme, differences have also been observed in human beings under such conditions as the following: The count varies in individuals with the constitution, nutrition, and manner of life; it varies with the time of day, showing a distinct diminution after meals; in the female it is decreased during menstruation, lactation and childbirth; drinking large quantities of water lowers it temporarily; it is lower in the aged than in those in middle life; fatigue may decrease it from 500,000 to 1,000,000 per cubic millimeter. On the other hand, the count is increased by thirst, profuse sweating, diarrhea, over-activity of the kidneys, starvation, and sleep.

The *diameter* of the erythrocytes in man is subject to wide variations, but in normal blood the size is very uniform, eighty per cent. of them measuring 7.5 to 8.5 microns. When extremely large they are

Fig. 683.—Red Blood Corpuscles of Different Vertebrate Animals. (Welker's models; from Boehm and von Davidoff.) ×1,000 diameters. *a*, From Proteus (salamander); *b*, from the frog; *c*, from a lizard; *d*, from a sparrow; *e*, from a camel; *f* and *g*, from the human being; *h*, from myoxus glis (dormouse); *i*, from a goat; *k*, from the musk-deer.

termed megalocytes, when small, microcytes. Their *thickness* at the outer denser portion is about one-fourth of the diameter, that is, 1.9 to 2 microns in a corpuscle 8 microns in diameter. The following is a list of the average diameters, and the number per cubic millimeter of the erythrocytes of various animals:

Source of blood.	Diameter, Micra.	No. per c. mm.
Man	7.5–8.5	5,000,000
Monkey	7.0	6,355,000
Hare	7.16	6,410,000
Guinea-pig	7.48	5,859,500
Dog	7.2	6,650,000
Cat	6.2	9,900,000
Horse	5.58	7,403,500
Spanish Goat	4.25	19,000,000
Musk Deer	2.5	

	Length.	Breadth.	
Chaffinch	11.9	6.8	
Chicken	12.1	7.2	
Dove	14.7	6.5	2,010,000
Duck	12.9	8.0	
Tortoise	21.2	12.45	629,000
Lizard	15.75	9.1	1,292,000
Snake	22.0	13.0	829,400
Frog	22.3	15.7	393,200
Toad	21.8	15.9	389,000
Triton	29.3	19.5	103,000
Salamander	37.8	23.8	80,000
Sturgeon	13.4	10.4	
Carp	17.7	10.1	

Leucocytes.—Physiologically the importance of the white blood-corpuscles is so many sided that they form the most interesting chapter in the study of blood. In mammalian blood, they are the only true cellular type among the blood elements, possessing a nucleus and all the other typical structures of a true cell. They are capable, in a restricted degree, of the same movements which are described as characteristic of the ameba. Instead of being flattened and of a pale straw color, as are the erythrocytes, these cells are more or less globular in shape, and perfectly colorless, even in layers. In further contradistinction

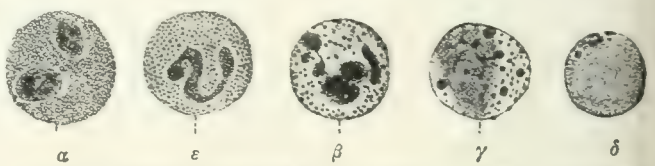


FIG. 685.—Ehrlich's Granules in Leucocytes. × 1,200. α, acidophile granules, relatively large and regularly arranged; ε, neutrophile granules; β, amphophile granules, not numerous and irregularly arranged; γ, mastzellen with granulations of unequal size; δ, basophile granulations. α, δ, and ε, from normal blood; γ, from leukæmic blood of man; β, from the blood of the guinea-pig. (From Boehm and von Davidoff, after H. F. Müller.)

FIG. 684.—Leucocytes from Normal Human Blood. × 1,200 diameters. (From Boehm and von Davidoff, after H. F. Müller.) a, Red blood disc; b, small mononuclear leucocyte; c, large mononuclear leucocyte; g, leucocyte with a nucleus of very irregular shape; d, e, f, leucocytes representing transitional forms between c and g.

to the red corpuscles, their small number is fully compensated by their exceptional power of regeneration.

In *size* the leucocytes range between three or four to fourteen microns in diameter. A fair average is ten or twelve microns, that is, about half again as large as the erythrocytes.

The *number* of the leucocytes, like most facts concerning them, varies widely under different conditions and at various times. In general it may be said to average about 8,000 per cubic millimeter, slightly less in females and more in males, or comparatively, 1 to 575-625 of the red cells. A slight variation from this proportion in either direction has no special clinical significance. When, however, the blood of an individual is found to contain less than 6,000 leucocytes per cubic millimeter, the condition is said to be that of *leucopenia*, and when more than 10,000, *leucocytosis*. Neither of these terms is to be considered as the name of a distinct disease, but each should be regarded as a symptom of some physiological or pathological bodily process.

A physiological leucocytosis is met with during digestion. It reaches its greatest height from two to three hours after a meal, and at that time a count of the white cells may show an increase of twenty-five to thirty per cent. Although the increase usually affects all of the white cells in about the same proportion in adults, it is not infrequent to find the percentage of polymorphonuclears somewhat raised. In young children the increase is more especially one in the number of lymphocytes.

In the latter part of pregnancy and during the puerperium, a slight leucocytosis is found, the polymorphonuclears showing the greatest increase. By the fourth or fifth day, however, the count usually returns to normal and does not appear to be influenced by lactation.

The blood of the new-born may show from 15,000 to 20,000 leucocytes per cubic millimeter for the first two days of extrauterine life. A gradual decline then takes place, until at the end of the second week the number is about 5,000 per cubic millimeter less, at which point it remains for the remainder of the first year. It then decreases very slowly until the average count of adult life is reached. During the first ten days the polymorphonuclears show the greatest deviation from the usual percentage, but beyond that time a relatively high lymphocyte count is the important factor. Leucocytosis of the newborn appears to be closely associated with plasmatic changes and active digestive processes.

The condition known as terminal leucocytosis is observed just before death, especially where it takes place slowly, and a moribund state has lasted for some time. It is probably due to peripheral stasis or to a terminal infection.

Among other physiological factors which may increase the number of leucocytes temporarily are massage, cold bathing, exercise, and electricity. They are more numerous in the veins than in the corresponding arteries, and are found in greatest number in the veins and capillaries of the spleen, liver, and glandular tissues, and least in the corresponding vessels of the skin, muscles, and general cellular tissues.

Although much importance has long been attached

to the white corpuscle count as an early means of diagnosing many of the acute fevers, inflammatory, malignant, and toxic conditions, during the past few years we have learned that it is also the best guide to the resistance of an individual toward infection. Briefly—given a mild infection and good resistance, a low white count is the result; given a severe infection with good resistance, a high count ensues; given a severe infection, with poor resistance, we find a low white count.

Leucopenia may result from starvation, senility, the use of certain drugs, and typhoid fever, pernicious and splenic anemia.

It must be borne in mind that the leucocytes are not all the same histologically and functionally. With the idea of systematizing the study of those found in normal blood, Ehrlich has divided them into two main groups, each of which is again subdivided, and this classification is now very generally followed. His grouping is as follows:

A. Lymphocytes.—Containing no granules in the cell substance, and although capable of ameboid changes of form, this ability is not characteristic and probably is not sufficient to cause locomotion.

(1) Small Lymphocytes.—About the size of the erythrocytes; the nucleus is large, concentrically placed, stains homogeneously, and the cytoplasm is reduced to a very small amount. They form twenty to twenty-five per cent. of the white corpuscles.

(2) Large Lymphocytes.—Two or three times as large as the small. The nucleus is placed eccentrically; the cytoplasm is non-granular, but is relatively more abundant than in the preceding variety. These forms constitute one per cent. or less of the white corpuscles.

B. Leucocytes.—Containing granules of different sorts in the cytoplasm, and with ameboid movement as a characteristic feature.

(1) Transition Forms (Mononuclear Leucocytes).—Large nucleus, more or less indented, and abundant, faintly granulated cytoplasm. The granules stain with neutral dyes. Their name implies that these leucocytes represent an intermediate stage between the large lymphocytes and the polynuclear leucocytes, but of late this view has been disputed by many observers. This form constitutes from two to ten per cent. of the total white cells.

(2) Polynuclear or Polymorphonuclear Leucocytes (Neutrophiles).—The nucleus is segmented into lobes connected by slender filaments. The cytoplasm is granular and especially ameboid. The granules are usually small in size and are neutrophilic. Typical cells of this variety form sixty to seventy-five per cent. of the total number of white corpuscles.

(3) Eosinophilic Leucocytes (Eosinophiles).—Similar to the preceding variety, except that the cytoplasm has numerous coarse granules which stain with acid dyes such as eosin. Eosinophiles make up from one-half to four per cent. of the white cells.

(4) Mast Cells (Basophiles).—Less than one per cent. of the total white corpuscles are of this type. They have a trilobed or polymorphous nucleus, but differ from the neutrophiles and eosinophiles in that the granules in the cytoplasm, which are very fine, stain only with the basic dyes such as thionin.

The Blood Platelets.—The platelets, thrombocytes, or plaques as they are often called, are colorless, round, jagged, or irregular protoplasmic structures, variable in size, ranging from one-half to five microns in diameter. In ordinary sections they are readily reduced to granular débris, but when well preserved and stained with Wright's stain, it appears that they have dark granular centers and clear peripheral zones. This peculiarity caused them to be interpreted formerly as small nucleated cells. J. H. Wright, however, who has given us the most useful information on the subject, shows conclusively that although they are formed elements, they cannot be considered true cells. He terms the outer clear zone ectoplasm and the inner granular portion endoplasm. He also credits them with ameboid movement.

Specially characteristic of these bodies is their tendency to clump together in refractile clusters from which strands of fibrin radiate. This circumstance greatly facilitates their distinction from other formed elements, but renders their enumeration very difficult. Estimates as to the *number* of platelets in one cubic millimeter of blood range between 180,000 and 778,000, no diluting fluid suitable for an accurate enumeration having been produced.

Their number appears to vary in direct proportion to the clotting power of the blood. It is increased, therefore, in such conditions as chlorosis, secondary anemia following hemorrhage, pneumonia, and in certain of the wasting diseases. In purpura hemorrhagica and in hemophilia, their number is extremely small.

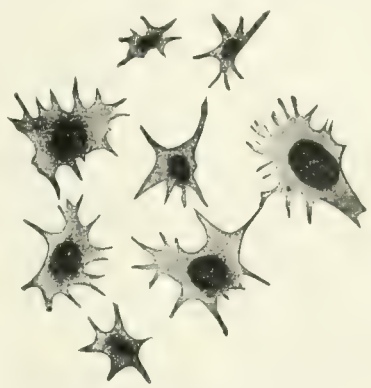


Fig. 686.—Blood Plates, showing Chromatic Centers regarded by some as Nuclei; and Exhibiting Ameboid Movement. (Schäfer, after Kopsch.)

Hemoconia.—Closely allied to the platelets is a fourth formed constituent designated by H. F. Müller as "hemoconia," "blood atoms" or "blood dust." It exists in the plasma as minute, colorless, highly refractile, spheroidal or hour-glass-shaped bodies, which resemble cocci or fat droplets. So far, however, all attempts to cultivate these particles on artificial media, thus stamping them as living organisms, have failed, as have those experiments intended to show that they are fatty in nature. They show a very active Brownian or molecular movement, and contrary to the behavior of the platelets, retain their shape for a very long time under observation without special precautions. Müller found them much diminished in hunger and cachexias, and increased in a case of morbus Addisonii.

Chemical Composition.—The analysis of blood as given by Hammarsten, is given below, 1,000 parts being taken. The individual constituents will be considered in discussing the chemistry of the various morphological components.

The Erythrocytes.—Halliburton gives the following composition for 1,000 parts of red corpuscles as they exist in the blood:

Water		688.0 parts
Solids	Organic	303.88 parts
	Inorganic	8.12 parts

and for 100 parts of dried corpuscles:

Protein	5.0 to 12 parts
Hemoglobin	86.0 to 94 parts
Lecithin	1.8 parts
Cholesterin	0.1 part

A part of the protein appears to be almost identical with the nucleoprotein of white corpuscles, which is thought to be the zymogen of the fibrin ferment. Another portion is doubtless a globulin. The mineral matter consists chiefly of the chlorides of potassium and sodium, and the phosphates of calcium and magnesium. In man and the higher apes the potassium salts are more abundant than those of sodium, but in some other animals, the reverse is true. Choles-

	Pig blood		Ox blood		Horse blood.		Dog blood.		Sheep blood.		Cat blood.		Rabbit blood		Human blood, man		Human blood, woman	
	Corpuscles	Serum	Corpuscles	Serum	Corpuscles	Serum	Corpuscles	Serum	Corpuscles	Serum	Corpuscles	Serum	Corpuscles	Serum	Corpuscles	Serum	Corpuscles	Serum
	153.09	564.91	325.5	674.5	397.7	602.7	142.8	577.2	319.2	680.8	434.0	566.0	372.1	627.9	513.02	486.98	306.24	693.76
Water	272.20	518.38	192.65	616.25	243.87	551.14	277.71	514.30	200.03	624.16	270.90	524.17	235.74	518.18	349.69	139.02	272.56	551.99
Solids	162.89	16.54	132.85	58.219	153.84	51.15	165.10	12.89	118.82	56.63	163.11	11.35	136.37	46.71	163.33	17.96	123.68	51.77
Hemoglobin	142.20		103.10		125.80		145.60		102.80		113.30		123.50					
Protein	8.35	38.36	20.89	48.901	20.05	42.65	2.36	34.05	12.80	16.56	11.62	33.16	1.56	33.63				
Sugar		0.684		0.708		0.90		0.74		0.708		0.860		1.026				
Cholesterin	0.218	0.251	1.10	0.885	0.26	0.31	0.56	0.37	1.17	0.891	0.556	0.339	0.268	0.343	Organic	bodies		
Lecithin	1.504	0.805	1.22	1.129	1.93	1.05	1.02	0.98	1.329	1.088	1.345	0.971	1.722	1.195	159.59	45.82	120.13	16.70
Fat		1.104		0.625		0.50		0.91		0.859		0.446		0.749				
Fatty acids	0.027	0.448			0.02	0.36		0.70		0.4908		0.282		0.507	Inorganic			
Phosphoric acid as nuclein	0.0455	0.0123	0.0178	0.0089	0.05	0.01	0.05	0.01	0.0235	0.0109	0.0083	0.009	0.010	0.015	3.71	1.14	3.5	5.07
Sodium		2.401		2.966		2.62		2.39		2.917		2.512		2.789			5	
Potassium	2.157	0.152	0.2351	0.1719	1.32	0.15	0.11	0.14	0.236	0.172	0.112	0.118	1.916	0.162	0.91	1.66	0.65	1.92
Oxide of iron	0.696		0.544		0.59		0.71		5.45		0.694		0.645		1.59	0.15	1.11	0.20
Calcium		0.0689		0.0805		0.07		0.06		0.089		0.062		0.072				
Magnesium	0.0656	0.0233	0.0656	0.03	0.01	0.03	0.03	0.03	0.006	0.027	0.035	0.024	0.029	0.028				
Chlorine	0.612	2.018	0.5901	2.488	0.18	2.20	0.60	2.31	0.575	2.546	0.455	2.360	0.460	2.438	0.44	1.42	0.36	0.14
Phosphoric acid	0.8056	0.1114	0.2392	0.1646	0.98	0.15	0.67	0.11	0.228	0.163	0.687	0.133	0.885	0.151				
Inorganic P_2O_5	0.7191	0.0296	0.1160	0.0571	0.76	0.05	0.54	0.05	0.088	0.057	0.515	0.040	0.645	0.040				

terin and lecithin belong to the group of fats, the latter one being specially designated a "phosphorized fat."

Hemoglobin, the most important constituent of the erythrocytes, is an extremely complex and variable histone-like globulin, globin, united with about four per cent. of an iron-containing pigment of constant composition, known as hematin. Although its composition varies to a certain extent in the different species, it is very widely distributed throughout the animal kingdom, being present in the red corpuscles of mammals, birds, reptiles, amphibia, fishes, and even many of the invertebrates. It is supposed to be almost identical with the pigment portion of chlorophyl or plant-green, by means of which the plants carry on their respiratory functions. Hemoglobin makes up from eighty-five to ninety-six per cent. of the organic constituents of the erythrocytes, about thirty-two per cent. of their weight, as they exist in the blood, and about fourteen per cent. of the blood's entire weight. Its molecule is of great size, the empirical formula, in the dog, being given as $C_{758}H_{1203}N_{195}S_3FeO_{218}$, making a molecular weight of 16,566.96, and in the ox $C_{759}H_{1208}N_{210}S_2FeO_{204}$, with a molecular weight of 16,531.67. Bunge asserts that so large a molecule, with its consequent relatively great momentum, is better able to transport the heavy iron atoms than would a small molecule. Moreover, it may be this large size of the molecule which renders hemoglobin so indiffusible, and which prevents its exosmosis from the capillaries.

FIG. 687.—Hemoglobin Crystals. *a*, Blood corpuscles from the general venous blood of man; *b*, crystals from the splenic vein of man; *c*, crystals from the heart blood of a cat; *d*, from the cervical veins of the guinea-pig; *e*, from the blood of a marmot; *f*, from the jugular vein of a squirrel. (After Frey, Histochemie des Menschen, 1874.)

The total amount of the hemoglobin has been suggested in connection with the structure of the erythrocytes. Its relative amount may be estimated clinically by means of instruments called hemoglobinometers or hemometers, nearly all of which require but a drop or two of blood. The method is usually that of color comparison with pieces of colored glass or paper whose color values have previously been determined in terms of hemoglobin, or of comparison with standard solutions of known hemoglobin content.

The condition in which the hemoglobin exists in the corpuscles is not entirely understood. For a long time it was thought that it was held in solution by the water of the corpuscles, but considering the slight degree to which hemoglobin is soluble, and the relatively small amount of water contained in the corpuscles, this idea has long since been discarded. Furthermore, even thin layers of corpuscles are opaque, which would not be true, were the pigment in simple solution. The transparency of hemoglobin in solution is well shown in the so-called "laky blood," where in some manner or other, the relations of the pigment within the corpuscle have been disturbed, so that it has escaped and become dissolved in the plasma. The process by which this is brought about is known as hemolysis, and may be induced by the addition of water, chloroform, ether, amyl-alcohol, bile or bile-salts, fatty acids, soaps, saponin, sapotoxin, snake venom, certain foreign sera, and considerable quantities of alkali. The same result may be brought about by such physical factors as alternate freezing and thawing, heat, and faradic electrical shocks.

Again, it may be demonstrated, by the use of crossed Nicol prisms, that hemoglobin does not exist in the erythrocytes as minute crystals, showing in the form of doubly refractive points, although this appearance may be noted when hemoglobin crystals obtained experimentally are observed. The highest powers of the microscope also fail to show any crystalline structures in the corpuscles.

The fact that lecithin and cholesterin constitute about thirty per cent. of the dry weight of the corpuscular stroma, a proportion found nowhere else in the body, except in the myelin of the nerve sheaths, led Hoppe-Seyler to advance the theory that the hemoglobin existed in some indefinite combination with these substances. It is now generally believed, however, that their purpose is that of assisting to maintain the characteristic permeability of the corpuscles. The assertion of Gamgee to the effect that the hemoglobin is present in an amorphous form, probably in an extremely unstable compound with some as yet unknown constituent, is, therefore, now almost universally accepted. He has shown that hemoglobin in an amorphous form may be obtained from its aqueous solution by means of electricity.

Hemoglobin has been analyzed by a number of different observers, and in numerous animals, but while the results vary somewhat as regards the proportions of the elements present, they all agree that it is made up of carbon, hydrogen, nitrogen, oxygen, sulphur, and iron. In addition to these, some observers state that hemoglobin, especially that of fishes, birds, and animals with nucleated erythrocytes, contain small amounts of phosphorus, probably taken from the nuclein of the corpuscles. Following are the average compositions as found by Jaquet and Preyer:

	Jaquet	Preyer
Carbon	53.91	54.00
Hydrogen	6.62	7.25
Nitrogen	15.98	16.25
Oxygen	22.62	21.45
Sulphur	0.54	0.63
Iron	0.33	0.42
	100.00	100.00

Although the so-called hemoglobin crystals obtained in the laboratory are usually really crystals of oxyhemoglobin, the pigment itself may be obtained in this form, but with varying degrees of difficulty in different animals. The hemoglobin from the red cells of the rat, guinea-pig, squirrel, cat, dog, and horse crystallizes readily in about the order named, while that of the rabbit, sheep, ox, frog, ape, and man is with considerable difficulty reduced to crystalline form. The crystals obtained show a beautiful red color, and contain water of crystallization, but differ in the amount of the latter, in shape, and in their solubility, according to the animal species from which they are derived. It is noteworthy that although it is a crystalline substance, hemoglobin acts much like colloidal substances, being practically non-dialyzable.

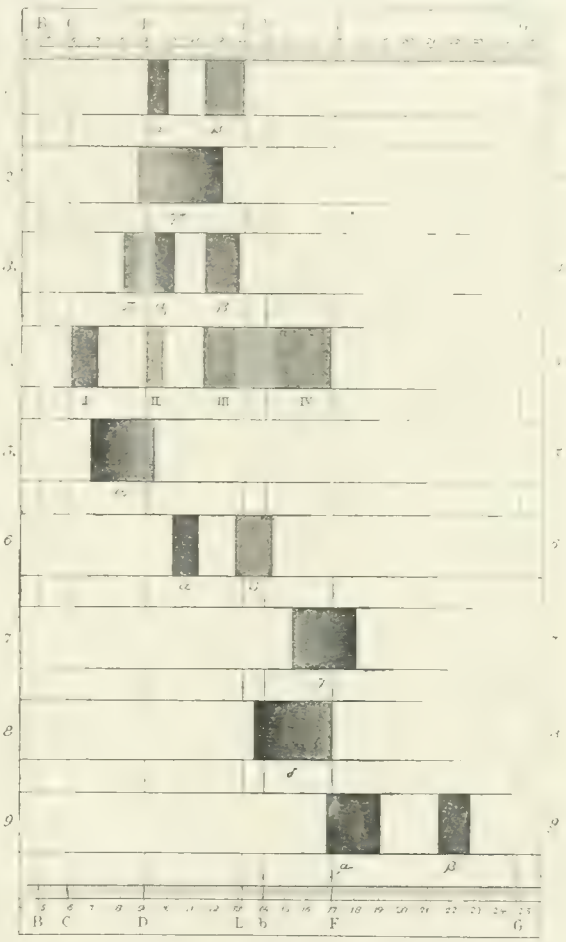


FIG. 688.—Spectrum. 1, Absorption spectrum of a solution of oxyhemoglobin; 2, absorption spectrum of a solution of hemoglobin, obtained by the action of an ammoniacal ferro-tartrate solution on an oxyhemoglobin solution; 3, absorption spectrum of a faintly alkaline solution of methemoglobin; 4, absorption spectrum of a solution of hematin in either containing oxalic acid; 5, absorption spectrum of an alkaline solution of hematin; 6, abcorption spectrum of an alkaline solution of hemochromogen, obtained by the action of an ammoniacal ferro-tartrate solution on an alkaline hematin solution; 7, absorption spectrum of an acid solution of urobilin; 8, absorption spectrum of an alkaline solution of urobilin after the addition of a zinc chloride solution; 9, absorption spectrum of a solution of lutein (ethereal extract of the egg yolk). (Hammarsten.)

The readiness with which hemoglobin from different animals dissolves, varies almost inversely from the ease with which it crystallizes. That from man is relatively soluble in water, dilute solutions of alcohol, of acids, of albumin, of the alkalies and their carbonates, and in sodium or ammonium phosphate. It is, however, insoluble in strong alcohol, ether, mineral acids, benzol, chloroform, carbon disulphide, and in the volatile and fatty oils. An excess of these substances will also precipitate hemoglobin from solution, as will heat and salts of the heavy metals.

It is probably due to some difference in molecular structure and differences in the amounts of water of crystallization contained that hemoglobin crystals from the blood of various animals assume different shapes. From the guinea-pig they take the form of four-sided pyramids. Those from the blood of the squirrel are plates of hexagonal shape, while crystallized hemoglobin from man and most of the higher vertebrates appears as rhombic plates, often so elongated as to simulate needles. Howell states that the pigment of horses' blood, which usually crystallizes in large rhombic prisms, may be made to give hexagonal crystals, by allowing it to putrefy, and that their form may still further be altered to rhombs by varying the temperature of the solutions.

The most characteristic, and at the same time the most interesting feature of hemoglobin from a functional standpoint is its power of absorbing various gases. It absorbs oxygen in considerable quantities, some writers claiming that one gram of coloring matter will take up 1.6 c.c of the gas, but gives it up when treated with deoxidizing agents. Accordingly, we distinguish between ordinary or reduced hemoglobin and oxyhemoglobin, but by means of oxidizing and reducing agents one can readily be converted into the other. Solutions of oxyhemoglobin show the bright red or scarlet color of arterial blood; those of reduced hemoglobin are much darker and of a purple or venous tint. Hemoglobin enters into combination with certain other gases, such as carbon monoxide, nitrogen dioxide, and hydrocyanic acid, more readily than with oxygen, and the well-known poisonous properties of these gases are due largely to their power of completely satisfying the affinities of the coloring matter to the exclusion of oxygen.

With the spectroscope, hemoglobin and each of its modifications gives absorption bands peculiar to itself. By the use of this method in conjunction with other tests, much may be learned from the blood as to certain pathological conditions, and even in very old stains it is possible to recognize the presence of blood. In order to obtain the best results, however, very dilute solutions must be used. The widths, intensities, and locations with regard to the Fraunhofer and special lines, of the absorption bands produced by solutions of hemoglobin and its modifications, are well shown by the accompanying spectral table.

Derivative Compounds of Hemoglobin.—The relations between hemoglobin, oxyhemoglobin, and some of the derivative compounds may be illustrated thus:

Hemoglobin { Globin; Hemochromogen } + O = Hematin; − Fe = Hematolin

Oxyhemoglobin { Globin; Hematin } + HCl = Hemin; − O = Hemochromogen; − Fe = Hematoporphyrin

Methemoglobin is much the same as oxyhemaglobin, except that the oxygen is combined differently, forming a more stable compound. It is found in sanguineous transudates, cystic fluids, and blood stains which have been exposed to the air for some time, giving them a brownish tint, and may even be formed within the vessels by the action of acetanilide, phenacetin, potassium chlorate, nitrites, etc. Experimentally it may be produced by the addition of such oxidizing substances as potassium permanganate or ferricyanide. Its crystals assume the form of needles. Methemoglobin cannot be dissociated by a vacuum, but will give up its oxygen by treatment with such reducing agents as ammonium sulphide.

Hematin ($C_{34}H_{33}N_4FeO_5$) is also found in old extravasations of blood. It is formed by hydrolysis of oxyhemoglobin and hemoglobin by acids and alkalies in the presence of oxygen. It is non-crystallizable, is of a dark brown color, and is easily soluble in alkalies and acidified alcohol.

Hemin ($C_{34}H_{33}O_4N_4FeCl$) is the hydrochloric acid ester of hematin, and is of great importance, as the obtaining of this substance in crystalline form (Teichmann's crystals) is the best chemical test for blood even in old clots or stains. This is accomplished by mixing a bit of the dry blood on a glass slide with a trace of sodium chloride and a drop of glacial acetic acid, and warming gently, when the characteristic dark brown rhombic plates and prisms will appear upon microscopic examination.

Fig. 689.—Hemin Crystals Magnified. (Preyer.)

Hematoporphyrin ($C_{32}H_{36}N_4O_6$) is iron-free hematin, and may be prepared by mixing blood with strong sulphuric acid. It is possibly isomeric with hematoidin and bilirubin.

Hemochromogen ($C_{34}H_{36}N_4FeO_5$) is formed when hemoglobin is decomposed by acids or alkalies in the absence of free oxygen, but is converted to hematin by oxidation. It may be obtained as crystals.

Hematoidin ($C_{16}H_{18}N_2O_3$) is a crystalline product found in old clots and extravasations, formed, doubtless, from the hemoglobin. It is said to be isomeric with the bile pigment bilirubin and with hematoporphyrin, but differs from the latter in showing no definite absorption bands in its spectrum.

Hematolin is the name given to an iron-free compound obtained by decomposing hematin in the absence of air.

Bile and Urinary Pigments.—These are thought to be derived, either directly or indirectly, from the hematin of the hemoglobin, by a process which involves the splitting off of the iron of its molecule. It is probable that much of the bile pigment is reabsorbed in the intestine for reelimination.

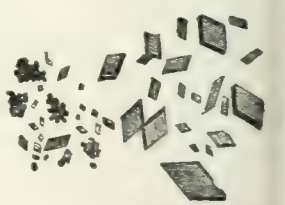


Fig. 690.—Hematoidin Crystals.

The Leucocytes.—No accurate analyses of the leucocytes have been reported. The numerous published statements regarding the chemical composition of pus cells are doubtless misleading, inasmuch as the latter are dead protoplasm. Wooldridge, however, gives an analysis of lymphoid tissue, which Halliburton considers similar to the composition of the leucocytes. This is as follows:

Water		885.1
Solids		114.9
		1,000.0
Nuclein	68.78	per cent.
Protein	1.76	
Histon	8.67	
Lecithin	7.51	
Fat	4.02	
Cholesterin	4.40	
Glycogen	0.80	
Total nitrogen		150.3
Total phosphorus		30.1

Among the proteins are alkali-albumin, paraglobulin, peptone, and a myosin-like albumin. The

enzymes said to be present are considered in the discussion of the functions of the leucocytes.

The Platelets.—According to Kossel and Lilienfeld, these bodies consist of a chemical combination of an albuminous substance with nuclein. By treatment with various reagents, such as artificial gastric juice, they can be differentiated into a homogeneous and non-refractive substance, which is subsequently dissolved, and an insoluble, highly refractive, granular portion, which gives the reactions of nucleins. Phosphorus can readily be demonstrated in the latter portion, and it is thought that this nucleoprotein may be identical with the substance known as nucleohiston. Ehrlich calls attention to the fact that the platelets contain glycogen, and that they are strongly alkaline in reaction.

Blood plasma is a colorless liquid obtained by removing the corpuscles without the assistance of coagulation. It normally constitutes from fifty-two to fifty-seven per cent. of the volume of the blood, the differences being due to factors which alter the number of corpuscles present. A number of methods have been devised for obtaining it free from the corpuscles, most of them depending upon agents which retard coagulation. This can be accomplished: By drawing the blood into a vessel containing some soluble oxalate in a proportion to make a solution of about 0.1 per cent. which withdraws the calcium, an ingredient necessary for coagulation; by drawing the blood into a paraffined receptacle, by which the blood is kept from the walls of the vessel; by injecting the animal, prior to the bleeding, with solutions of pepsin, trypsin, snake-venom, leech-extract, or peptone, thereby provoking some reaction whose products prevent coagulation; by the addition of sodium fluoride; by adding one part of a saturated solution of magnesium sulphate, or the same amount of a ten-per-cent. sodium chloride solution, to four parts of blood; or by drawing the blood into an ice-cold vessel and placing it immediately on ice. The corpuscles slowly settle to the bottom of the vessel, leaving the clear zone of plasma above. The corpuscles may be separated also by the use of the hematocrit, a form of centrifuge.

The *serum* is a viscid liquid, varying in color from a pale yellow or straw-color in man, to a deep amber yellow, as obtained from the horse. It is the portion of the blood squeezed out by the contraction of the clot, and is more alkaline than the plasma. It further differs from the plasma in containing an abundance of fibrin ferment, but no fibrinogen. It is ordinarily clear, but after a meal may be opalescent because of the contained fat. The yellow coloring matter of serum is a lipochrome, a member of the lutein group, and is soluble in alcohol. In the serum of the horse, other pigments are found, notably bilirubin.

Hammarsten gives as the average composition of the plasma of the horse, the following, 1,000 parts being the basis. Similar analyses by Hoppe-Seyler and Simon are given for comparison:

	Simon.	Hoppe-Seyler.	Hammarsten.
Water	910.5	908.4	917.6
Solids	89.5	91.6	82.4
Total proteins	69.5	77.6	69.5
Fibrin	6.5	10.1	6.5
Serum globulin	38.5	67.5	38.4
Serum albumin	24.5		24.6
Fat	2.5	1.2	
Extractives	9.0	4.7	12.9
Mineral salts	8.5	8.1	

Inorganic Substances in Plasma.—Plasma consists of about ninety per cent. of water, the inorganic salts occurring to the extent of about 0.8 per cent. The principal salt is sodium chloride. Sodium carbonate is probably the next most abundant, and it is to this salt that the plasma owes its alkalinity and its power of absorbing carbon dioxide. In addition to these small amounts of the following salts appear to be present: potassium chloride, potassium sulphate, calcium phosphate, sodium phosphate, magnesium phosphate, and probably calcium chloride.

Proteins.—The proteins of plasma are: one or more closely allied albumins called serum-albumins; two globulins, namely, serum globulin and fibrinogen; one or more nucleoproteins. Blood normally contains neither albumose nor peptones. Although differing somewhat from the figures given by other observers, a table by Howell showing the amounts of several proteins in grams per 100 c.c. of plasma is given below:

	Man.	Dog.	Sheep.	Horse.	Pig.
Total proteins	7.26	6.03	7.29	8.04	8.05
Serum-albumin	4.01	3.17	3.83	2.80	4.42
Serum-globulin	2.83	2.23	3.00	4.79	2.98
Fibrinogen	0.42	0.60	0.46	0.45	0.65

The *albumins* of plasma are also found in the serum after coagulation, and it is probably for this reason that they are called serum-albumins. Halliburton names three varieties, basing the division upon their susceptibility to heat coagulation: α-albumin, coagulating at 72° to 75° C.; β-albumin at 77° to 78° C.; and γ-albumin at 83° to 86° C. In man and all mammals and birds investigated, except the horse, ox, and sheep, he found all three varieties; in the latter animals the α-albumin was absent. In the plasma of the reptiles, amphibia, and fishes examined, on the other hand, only the α-albumin was found.

The *globulins* of plasma consist of serum-globulin, sometimes called paraglobulin, and fibrinogen. The former coagulates at a temperature of 75° C. This degree of coagulation is almost constant for the animals examined. Its molecular composition has been represented (Schmiedeberg) by the formula $C_{117}H_{182}N_{30}SO_{38}+1/2H_2O$. Hammarsten gives its percentage composition as: C, 52.71; H, 7.01; N, 15.85; S, 1.11; O, 23,32.

The *fibrinogen* is the substance which, under proper conditions, gives rise to an insoluble protein, fibrin, whose formation is the necessary feature in the clotting of blood. It coagulates at a temperature of 56° to 60° C., much lower than does globulin. It is further distinguished from the latter in being completely precipitated by saturation with sodium chloride, as well as with magnesium sulphate, whereas globulin is only partially thrown down. Schmiedeberg gives it a molecular formula of $C_{105}H_{162}N_{30}SO_{34}$. Its percentage composition is, according to Hammarsten: C, 52.93; H, 6.90; N, 16.66; S, 1.25; O, 22.26. Schmidt, Pekelharing, and others assert that instead of being a simple substance, it is either a loose combination or a mixture of fibrin, fibrin-globulin, and probably a nucleoprotein.

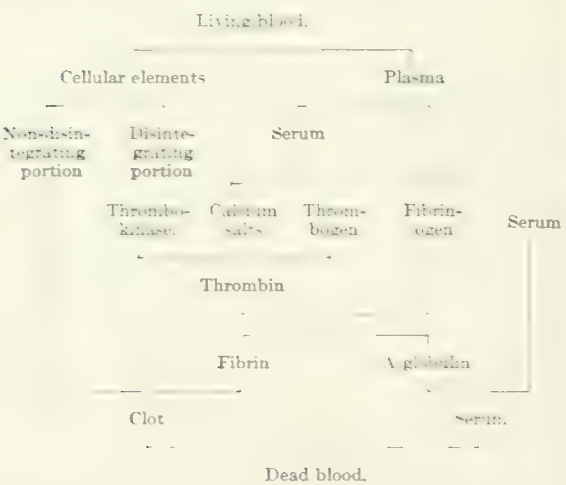
Fibrinogen is used up in the process of coagulation, and is therefore not found in serum. It is, however, always present in blood and lymph, although in smaller amounts than the other proteins, and usually in pleural, pericardial, hydrocele, and ascitic effusions. No conclusive reports have been made as to its seat of origin. Experiments by Dastre, Mathews, Bizzozero and Doyen show that by successive bleedings, defibrinations, and reinjections, the fibrinogen may be completely removed from the blood of cats and dogs, only to be redeveloped to the normal or a greater amount in a day or two. Because of the fact that it does not reappear in the blood after removal of the liver or the small and large intestines, and that the blood of the mesenteric, portal, and hepatic veins

contains a relatively high percentage of fibrinogen, it is thought by some to arise in these organs. The pancreas, spleen, kidneys, muscles, and reproductive organs apparently take no part in its production. Because of the presence of a nucleoprotein in its make-up, it has further been suggested that fibrinogen is derived from blood platelets and from nuclei of disintegrating leucocytes, or the extruded nuclei of newly formed erythrocytes.

Fibrin is a protein, insoluble in water, alcohol, and ether, which exists not as such in the blood, but forms during the process of coagulation. The blood-corpuscles take no active part in the formation of the clot, but are simply entangled in its meshes. A quick method of obtaining fibrin is to stir or whip the blood with twigs immediately after its withdrawal. Under these conditions it does not entangle the corpuscles, but adheres to the twigs as a white stringy mass whose interlacing threads show a strong tendency to retract. It is because of the latter fact that the blood clot concentrates and squeezes the serum from its interior.

Hammarsten gives the percentage elementary composition of fibrin as: C, 52.68; H, 6.83; N, 16.91; S, 1.10; O, 22.48. It is slowly soluble in five to ten per cent. solutions of sodium chloride, sodium sulphate, potassium nitrate, magnesium sulphate, ammonium sulphate, and in iodides and solutions of urea. Dilute acids and 0.1 per cent. solutions of sodium or ammonium hydrate reduce it to a gelatinous mass, which is soluble after a few days.

For a detailed discussion of the probable manner of fibrin formation, the reader is referred to the article on *Coagulation*. The relations of the different parts of the blood to each other, including the factors concerned in coagulation, may, for present purposes, best be represented graphically as follows:



Regarding the *nucleoprotein* of the plasma, it may be said that its presence is disputed by a number of reliable observers. By those who hold this view, it is claimed that the substance described as nucleoprotein is in reality a combination or mixture of protein and lecithin, the latter being brought down by the protein during the process of precipitation. They further state that the phosphorus, the presence of which has given rise to the belief that nucleoprotein does exist as such in the plasma, is usually removable by boiling with alcohol. Others, notably Freund and Joachim among the more recent investigators, still maintain, however, that nucleoprotein is contained in the plasma. It is supposed to be a product of a partial disintegration of the platelets, possibly the erythrocytes, and the nuclei of leucocytes, which takes place when the blood is shed. Nucleoprotein is thought by some to be an important factor in the development of fibrin and is not found in pathological effusions where few or no cellular elements are present. Under these conditions, there is no coagulation, although such fluids usually contain fibrinogen.

Nitrogenous Extractives.—The most abundant of these is urea, occurring to the extent of from 0.02 to 0.05 per cent. It is said (Drechsel) to be produced in the muscles and liver from ammonium carbonate, a product of tissue protein catabolism, and is most abundant in the portal and hepatic veins. Uric acid, creatin, creatinin, xanthin, hypoxanthin, leucine, tyrosine, glycuronic and other amido-acids occur in smaller amounts. The presence of lecithin has already been mentioned. Jecorin is said to be a constant constituent of plasma. It will reduce Fehling's solution, and is soluble in ether, but is not fermentable. It is more plentiful in venous than in arterial blood.

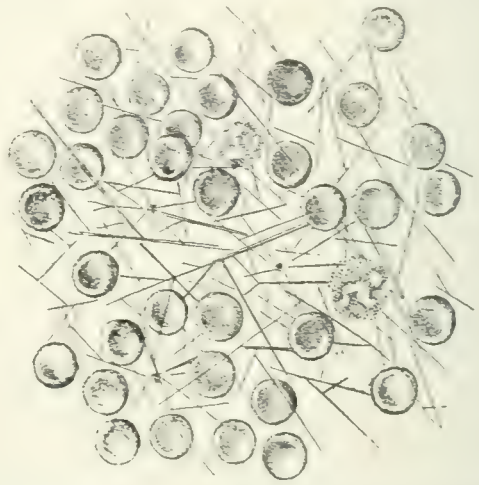


Fig. 691.—Hyperinosis Showing Marked Increase in the Density of the Fibrin Network. (Da Costa's Hematology, P. Blakiston's Son & Co., 1905.)

Non-Nitrogenous Extractives.—These consist of the carbohydrates—dextrose, glycogen, and an animal gum—and fats, soaps, cholesterin, a lipochrome, and lactic acid.

Dextrose is always present in the plasma, even in starving animals. In man it is found normally to the extent of 1.2 parts per 1,000, and in the dog from 1.1 to 1.5 parts per 1,000. It seems to be present in nearly equal amounts in all parts of the blood except in that of the portal vein, where it is markedly increased during the digestion of carbohydrate food. Differences in the quantity of dextrose in the plasma in other parts of the body, under various physiological conditions, have been reported, but it is thought that such findings were the result of experimental errors. The total amount, however, is increased as the result of hemorrhage, due perhaps to an increase of lymph, which contains more sugar than does blood; or as an effect of nervous influences which stimulate the production of sugar from the liver glycogen. It is also increased in diabetes, whether this be a result of disease or of puncture of the floor of the fourth ventricle. Hyperglycemia, that is, a condition in which the amount of sugar in the blood is increased to more than 0.25 or 0.3 per cent., is promptly followed by glycosuria.

A very slight amount of *glycogen* may be obtained from the plasma of fresh blood. It is undoubtedly derived from disintegrated leucocytes, which, as is well known, contain it. Kaufmann has pointed out that the quantity of glycogen is increased in the blood

upon the removal of the pancreas. This is thought to be due to the loss of the glycolytic ferment of the pancreas, which normally assists in the combustion of glycogen.

Freund has obtained from the plasma a carbohydrate resembling that described by Landwehr under the name of *animal gum*. Its formula is given as $(C_6H_{10}O_5)_n$ and it is converted by boiling with dilute mineral acids into a substance which reduces Fehling's solution, but is not fermentable nor rotary for polarized light.

Fats.—These consist of tristearin, triolein, and tripalmitin. They are present in the plasma in but small and variable quantity (from 0.2 to 1 per cent.), being most abundant after a meal containing much fat. The plasma or serum may then have a milky appearance on account of the admixture with fat-containing chyle. A small amount may exist in the form of soap. The fatty acids also appear to be partly in combination with cholesterin. Hoppe-Seyler states that the cholesterin in blood plasma amounts to about 0.05 gram per 100 c.c. of blood.

Lactic acid is said by Gaglio to be a constant constituent of the normal plasma. Other observers have confirmed his findings and have also demonstrated it in small quantities in the corpuscles. Sarcolactic acid is known to be a product of muscle action, and is in combination with ammonia and sodium in the blood, ammonium lactate being the form in which the products of protein catabolism are carried to the liver, according to Schäfer, for ureagenesis. Experimentally, it is increased by the intravenous injection of dextrose.

The *ferments* and *gases* of the plasma will be considered under the heading, "Functions." In addition to the gases mentioned, however, there is a small amount (1.8 to 2.5 per cent.) of nitrogen simply dissolved in the plasma, but it apparently has no respiratory function.

Origin of Blood-corpuscles.—The blood-corpuscles, like the body itself, fulfill the allotted round of life and then die. They rise, perform their functions for a time, and then disappear. But although the place and mode of their origin, the seat of their destruction and decay, and the length of their life have been the subject of active research and still more active discussion for many years, much still remains unsettled. The problem concerns not only the first blood cells in the embryo and their life history, but also the origin and development of new cells during later fetal and postnatal life of the individual. It has been deemed advisable, therefore, to treat separately the two modes of origin of both the red and the white corpuscles, taking up their ultimate fate in a distinct section. Because of the wide range which such a discussion would necessarily cover, a description of the formation of the plasma has been omitted.

Fig. 692.—Section across Yolk-sac, Showing Blood-vessels and Nucleated Red Blood Corpuscles Forming in Its Mesoblastic Layer. (Keith, after Selenka.)

Prenatal Origin of Erythrocytes.—Most hematologists and histologists now agree that the first red corpuscles are developed in the area vasculosa, a portion of the mesoblastic tissue, which is outside the embryo. Within certain of the cells, hemoglobin is developed, giving rise to patches known as "blood islands." Later, outgrowths from these form the blood-vessels of the embryo, by joining similar projections within the growing body. The method of formation of both the blood-vessels and corpuscles is, however, a disputed question.

Reichert and Kölliker claimed that the cells of the area vasculosa develop into cords of cells which form a communicating network, and that the peripheral cells of these cords later form the walls of the future blood-vessels, while the innermost ones, becoming pigmented by hemoglobin, remain attached to those outermost in minute groups. At the same time a fluid, which is to be the future plasma, appears among the small cell masses. As the heart develops and begins its rhythmic contractions this fluid is set in motion, gradually detaching the individual cells, which become the first red corpuscles. These primitive corpuscles, which are nucleated, together with the still attached cells, undergo mitosis, thereby increasing the number in the circulating blood. The process of detachment and cell division have been actually observed in the transparent embryos of certain fishes.

Schäfer and others, on the other hand, contend that the blood-vessels are formed by the anastomosing processes sent out by certain cells of the vascular area. They claim that a liquefaction of certain portions of the cytoplasm takes place, forming the future plasma. Meanwhile extensive division of the nucleus also occurs, the resulting nuclei being surrounded by small portions of the remaining cytoplasm. As the vessels develop and the heart becomes active, these small masses of protoplasm become pigmented with hemoglobin and begin circulating as red corpuscles. The primary red cells thus formed are capable of ameboid movement and of cell division, resembling leucocytes except in color and in the absence of granulation.

Howell describes two types of nucleated red corpuscles in the embryo, one a large oval cell, sometimes biconcave, sometimes biconvex, the other a circular variety, about the size of the typical adult red corpuscle. He designates the large type as ancestral corpuscles, and claims that the circular variety represents a modification of the other type, which so closely resembles those seen in the ancestors of the mammalia. These modified cells are converted into biconcave discs by the loss of their nuclei while circulating in the blood.

In the development of the embryo a point is soon reached when the formation of primitive blood-vessels ceases, the future vascular system being produced by the growth of the structures already formed. As red corpuscles are continually disintegrating, and as the growth of the circulatory system necessitates a constant increase in the volume of the blood and a corresponding increase in the number of its formed elements, it is obvious that from this point some other means of their production must exist. Since the multiplication of nucleated red corpuscles takes place by mitotic division, the activity of the various organs along lines of hemopoiesis has been rated from the relative number of karyokinetic figures which they contain.

At first the liver seems to be the important organ in the performance of this function, although various observers disagree as to the manner in which it takes place. Howell states that the blood-forming cells are arranged in cords lying between the columns of the true liver cells, and that the peripheral cells of these strings undergo structural alterations, becoming the endothelial lining of the liver capillaries, while the inner cells are set free as red corpuscles. Kölliker demonstrated, to his own satisfaction at least, that the nucleated erythrocytes arose from certain white corpuscles in the developing vessels of the liver, that hemoglobin was formed within them, and that they became mature red corpuscles by the loss of their nuclei. Neumann thinks that they are formed by the division of the nuclei together with portions of

the cytoplasm within certain large cells of the embryonic liver.

The liver, however, later takes up other work, and the process of red blood-corpuscle production there gradually ceases. The next organ to take up the hematopoietic function appears to be the spleen. Here the process, in nature much like that which takes place in the liver, commences at about the fifth month of intrauterine life and apparently persists

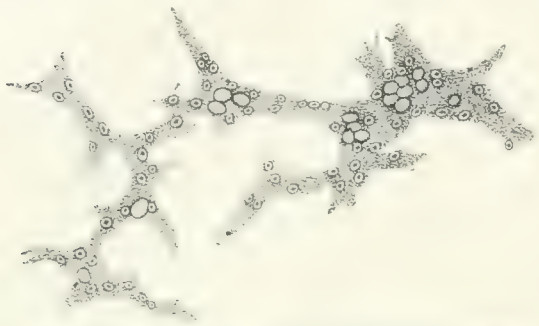


Fig. 693. Part of the Network of Developing Blood-vessels in the Vascular Area of the Guinea-pig. (After Schäfer.)

until the work is entirely taken over by the red marrow of the bones, probably at about the time of birth.

Both Schäfer and Ranvier ascribe the formation of red corpuscles during late intrauterine life to large connective-tissue cells called angioblasts or vasoformative cells. The process consists of the development of hemoglobin in the cell cytoplasm and the subsequent breaking up of this pigmented substance into minute masses, at first variable in size, but later nearly uniformly the size of mature red corpuscles. The angioblastic cells anastomose by means of their processes, which later, by the liquefaction of some of the remaining cytoplasm, become hollow

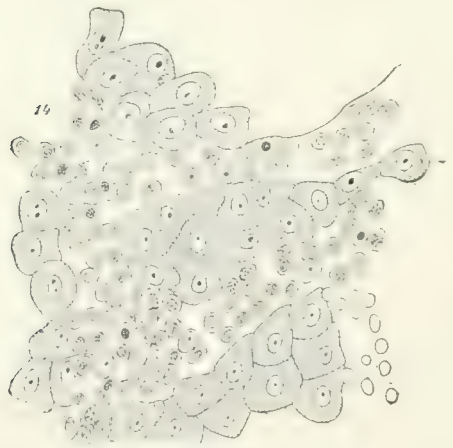


Fig. 694.—Section of the Liver of a Fetal Cat, 2.7 Centimeters, Showing the Development of the Liver Vessels and the Nucleated Red Corpuscles. To the right of the figure the newly formed vessel contains a number of non-nucleated red corpuscles. (After Howell.)

tubes, joining the already formed vascular system as new vessels and thereby allowing the contained fluid and corpuscles to enter the general circulation. This theory apparently does not recognize nucleated red cells as being the precursors of all mature erythrocytes inasmuch as the cytoplasm of the angioblast is the only portion of the cell concerned in the process, according to Schäfer's description.

It is of interest to note in this connection that the earliest red corpuscles to appear in the human embryo are of the nucleated type. After the fourth week, however, non-nucleated forms begin to appear, and by the third month the nucleated varieties constitute only one-sixth to one-eighth of the total number of corpuscles. The diminution after this is less rapid, but it is only at about the time of birth that they disappear from the blood altogether.

The question of the manner in which the nucleated red corpuscles become converted into the non-nucleated variety, typical of mammalian blood, is a much disputed one. Howell and others claim to have observed the extrusion of the nucleus in a free condition, and this theory is supported by the fact that free nuclei which have presumably been extruded from corpuscles are frequently seen in sections, and that cells in all stages of nuclear extrusion may be observed in specimens procured after extensive bleeding when there is a rapid regeneration of the blood constituents. Malassez thinks that the original nucleated cells persist throughout life and that the non-nucleated discs arise by the setting free of a portion of the pigmented cytoplasm by a process of budding and subsequent constriction. The view which to-day

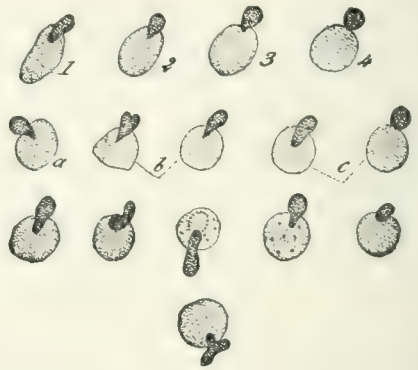


Fig. 695.—The Manner in Which the Nucleus Escapes from the Nucleated Red Corpuscles, according to Howell. 1, 2, 3, 4, represent different stages of extrusion noticed upon the living corpuscles; *a*, specimen from the circulating blood of an adult cat, bled four times; *b*, specimens from the circulating blood of a kitten forty days old, bled twice; *c*, specimens from the blood of a fetal cat nine centimeters long. Others from the marrow of an adult cat, two of the figures showing the granules which have been interpreted by some as a sign of the disintegration of the nucleus. (After Howell.)

claims the most adherents, however, is that originally expressed by Kölliker and later extended somewhat by Neumann. According to this view the nucleus becomes small, more homogeneous, and later notched or indented, while the cell as a whole gradually becomes flattened. As a later stage, the nucleus undergoes fragmentation, and the particles are slowly absorbed by the cytoplasm, leaving the typical non-nucleated red blood corpuscle. From a chemical standpoint, there seems to be reason for placing some faith in this theory, inasmuch as nuclein can be demonstrated in considerable quantities in adult erythrocytes.

Postnatal Origin of Erythrocytes.—As has been suggested in the previous section, the hemopoietic function of the spleen probably ceases at, or shortly after, birth at full term, and there is much evidence to show that this organ does not again play a part in red corpuscle formation, except possibly after severe hemorrhage, or in such conditions as pernicious anemia, where there is an abnormal demand for new corpuscles. Regarding the place of origin after birth, it is now generally admitted that the red bone marrow is the seat of their most abundant production.

Their formation in this location doubtless commences during the last few weeks of intrauterine life, overlapping somewhat the diminishing efforts of the spleen in this direction. Here again, however, there is

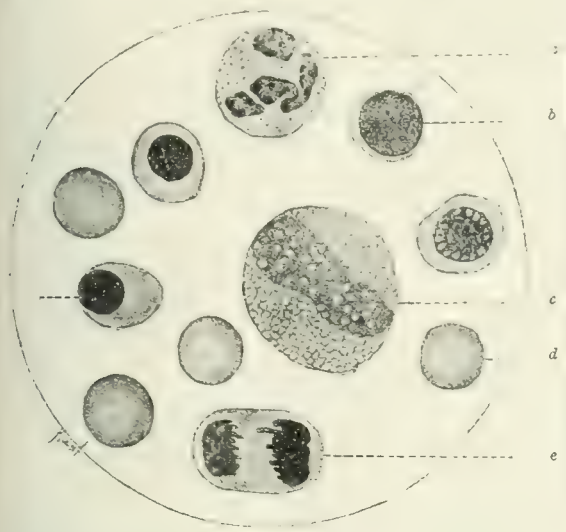


Fig. 696.—From the Bone Marrow of the Dog. × 1,200 times. (From Boehm and von Davidoff, after H. F. Müller.) *a*, Mastzelle; *b*, lymphocyte; *c*, leucocyte with acidophile granules; *d*, non-nucleated blood corpuscle; *e*, nucleated red corpuscle in the act of dividing; *f*, nucleated red corpuscle.

much diversity of opinion as to the manner in which they arise.

Three types of cell have been described by various observers as being the forerunners of the nucleated red corpuscles of the bone marrow. The first is a leucocytic cell, resembling greatly an immature erythrocyte, save that it contains no hemoglobin, but differing from ordinary blood leucocytes in having no phagocytic or ameboid properties, and in being more homogeneous in appearance. The second is the ordinary marrow cell, somewhat larger than the above and containing a prominent vesicular oval nucleus with one or two nucleoli. The cytoplasm of these cells may be filled with coarse granules, the nucleus may be elongated, horseshoe-shaped, or even coiled upon itself. The so-called giant cells, the third type, are considerably larger than the other two, and contain a single nucleus which may also be elongated, or coiled so as to simulate the appearance of multiple nuclei on section.

Neumann holds that the nucleated red cells of the bone marrow arise from the unpigmented, or first type of cell described above. Neumann and Löwit, incidentally, limit the use of the term erythroblast to this cell. Foá and Salvioli state that the giant cell described by Bizzozero as having a budding nucleus made up of numerous segments connected by a thin filament, is the immediate predecessor of the nucleated red corpuscle. These hematoblasts, as they are termed, develop into nucleated red cells by breaking up into numerous smaller cells, each containing a segment of the convoluted nucleus and the subsequent development of hemoglobin. Malassez expresses the view that they are derived from the ordinary marrow cell by passing through several stages in which the cells ultimately decrease in size, develop hemoglobin and become granulated. Howell entertains much the same idea, except that he describes a series of stages through which they pass by karyokinesis before the mature nucleated red cell is evolved.

Many other theories are still maintained as to the origin of the nucleated erythrocytes of the marrow, among which may be mentioned that of Osler. He contends that they arise from still another type of hyaline cell of the bone marrow. Bizzozero, Schäfer, and others hold that they are the result of mitotic division of similar embryonic cells which are brought from the liver and spleen when the red marrow begins to develop. Obrastzow believes that the red blood discs are formed from the nuclei of hyaline cells of the red marrow, without, however, passing through the nucleated stage. Löwit supposes that the parent cells arise in the lymphatic glands and spleen and are later carried to the red marrow to be transformed into nucleated erythrocytes. Some observers state that the seat of red-corpuscle formation is in the line of ossification between growing bone and its hyaline cartilage, and even Hayem's theory, that they arise from the blood platelets, still has a few adherents.

As can be seen from the preceding discussion, the study of the postnatal origin of the erythrocytes is still open to extensive research. We know, however, that the red blood cells of the marrow are nucleated, are of variable size, and are capable of active ameboid movement. They undergo regeneration for the purpose of supplying substitutes for their worn-out predecessors, and to replenish the blood after hemorrhage, and in diseases involving corpuscle destruction, by karyokinesis. It is further probable that in cases of grave emergency, the red marrow, which is normally confined to the flat bones and the ends of the mature long ones, extends to the shafts of the latter, and that even the spleen may resume its former hemopoietic function.

Fate of the Erythrocytes.—Just when and how the

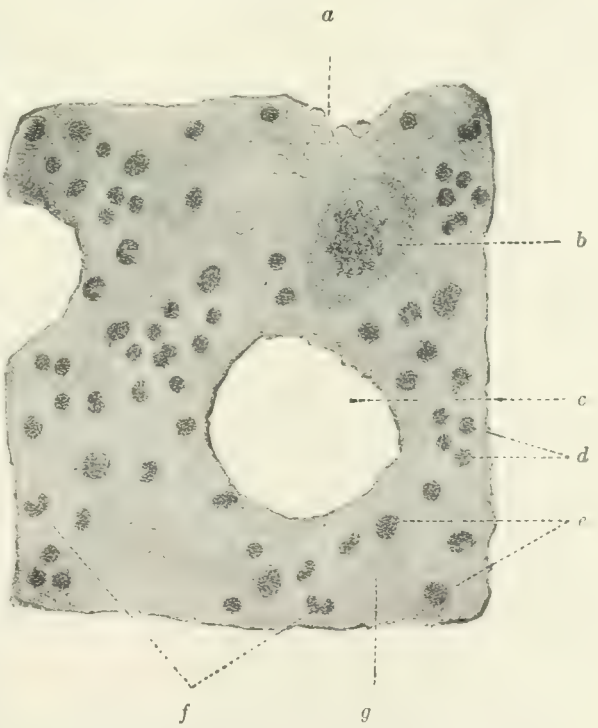


Fig. 697.—Section of Red Bone-marrow from Rabbit's Femur. *a*, Erythrocytes; *b*, myeloplax; *c*, fat space; *d*, erythroblasts; *e*, myelocytes; *f*, reticulum; *g*, leucocytes. (After Bailey and Miller.)

erythrocytes are broken up is not definitely known. Considering the fact, however, that hemoglobin is the mother substance from which the bile and a portion

of the urinary pigments are formed, and that these pigments are being continually excreted, it is not probable that any particular corpuscle lives for a great while in the circulation. Howell places the limit of life of a given red cell at ten days, basing his conclusions mathematically upon the amount of hemoglobin necessary to form the quantity of bile obtained daily from biliary fistulæ, as compared with the estimated hemoglobin content of the blood.

Because of the histological fact that red corpuscles in various stages of disintegration can sometimes be demonstrated in specimens of spleen-tissue and lymph glands, within certain large cells called macrophages, it has been suggested that the destructive process takes place in these organs. The spleen tissue also contains a certain amount of iron. Against this

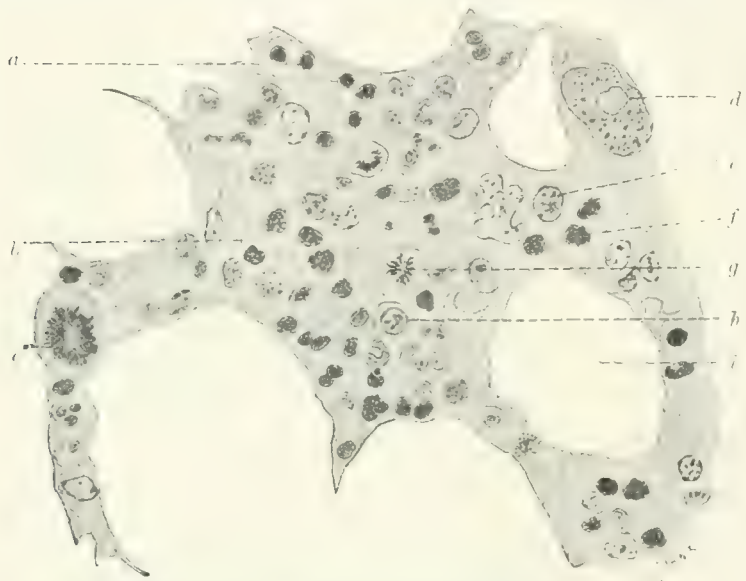


FIG. 698.—A Section Through the Red Bone-marrow of Man. × 680. *a*, *f*, Normoblasts; *b*, reticulum; *c*, mitosis in a giant cell; *d*, giant cell; *e*, *h*, myelocytes; *g*, mitosis; *i*, space containing fat cells. (Boehm u. von Davidoff, Lehrbuch der Histologie, Wiesbaden, 1903.)

idea, however, is the objection that the small number of erythrocyte-containing leucocytes in the spleen is not at all consistent with the number that should be in evidence were the destruction taking place there to any great extent. Furthermore, removal of the spleen does not appear to have any effect upon the rate of red corpuscle dissolution. We have come to believe, therefore, that the phenomenon of ingestion by the macrophages occurs only when the red cells are in a state of rest while the ameboid movements of the leucocytes continue, that is, after death. It is more probable that no particular organ or tissue is endowed with the corpuscle destroying function, but that they may disintegrate in any part of the circulation. The liberated hemoglobin appears to be carried to the liver, whose cells, by means of an internal secretion, remove the iron, thereby conserving it for future body use, and excrete the pigment portion as the coloring matter of the bile, and in part at least, of the urine.

Prenatal Origin of Leucocytes.—The leucocytes begin to appear in the blood of the embryo at, or shortly before the fifth month, at which time the development of the red corpuscles is well under way. It is not probable, therefore, that they are formed in the organs from which the first erythrocytes arise. In fact, most authors agree that the white corpuscles are developed in tissues entirely outside the blood-vessels, reaching the circulation by virtue of their ameboid movement and by the lymph stream. The first white corpuscles observed conform roughly to the two general types seen after birth, the first uninuclear and non-granular, and the second multinuclear and faintly granular.

Ziegler states that the first leucocytes arise from cells which have become detached from the mesoderm. He regards the lymphatic glands as the source of the white corpuscles during later intrauterine, and throughout extrauterine life, claiming that these organs are portions of embryonic mesodermic tissue set aside to carry on the production. According to his observations, the small lymphocyte is the earliest to appear, the other varieties representing advanced stages in the development of this cell. Schäfer similarly regards the leucocytes as cells separated from the mesoderm.

In late intrauterine life, the liver appears to play a part in leucocyte production. This function, however, is not assumed by the liver until after its erythrocyte formation has ceased, according to Löwit, and acts only as a temporary reinforcement to the slowly developing lymphatic glands. Although the spleen may be a factor in leucocyte formation, especially in connection with the lymphocytes, as the fetus nears full term the lymphatic glands and red bone marrow appear to be capable of supplying the demand for new cells. The process of leucocyte formation in the lymph glands is probably one of mitotic division of some of the cells of these structures. It has also been suggested that white corpuscles are formed in late intrauterine life in the intestinal epithelium or in the tissues underlying it.

Postnatal Origin of Leucocytes.—The extensive researches of Ehrlich, Kurloff, and others show quite conclusively that throughout extrauterine life, the chief sources of leucocyte production are the lymphatic tissues and the red marrow of bone. Experimental splenectomy has demonstrated that in man, at least, the loss of this organ, which was formerly considered of great importance, especially in lymphocyte formation, is more than offset by a compensatory hypertrophy of the lymphatic glands, and that the spleen is relatively unimportant in that respect. Löwit describes the leucocytes as arising from leucoblastic cells in lymphoid tissue, the spleen, and bone marrow, arriving in the blood as the small or young variety of lymphocyte, incapable of ameboid movement, and having a prominent vesicular nucleus, surrounded by a small rim of non-granular cytoplasm. He holds that the differences in size, shape of nucleus, and appearance of cytoplasm observed in the several varieties result from a change which rapidly occurs in the venous blood before it reaches the arterial side of the circulation. This view has been disputed by Flemming, Bannworth, and others, who claim that multiplication of leucocytes takes place by a true mitotic division. Instead of regarding the polymorphonuclear and multinuclear types as cells undergoing cell division, they consider these varieties cells whose nuclei are undergoing fragmentation previous to the disintegration of the cell.

Ehrlich's views, based upon extensive observations during various diseased conditions, are to the effect that the two general types of leucocytes, the granular and non-granular, are derived respectively from the bone marrow and the lymphatic glands. He maintains that these two sources of origin are entirely in-

dependent of each other, and that each confines itself to the production of its particular type of cell. He admits the possibility of lymphocytes normally arising from the bone marrow in small numbers, but contends that this phenomenon is due to the presence of lymphatic tissue in the marrow.

Among the granular cells, Ehrlich distinguishes two general varieties. The first are those containing "special" granules, in other words, granules which constitute a characteristic for certain animal species. Man and monkey, for example, have neutrophilic granulation. The other variety of cells contains granules which are found in the whole vertebrate series from frog to man, and which are not characteristic of any one species of animal. These are the eosinophiles, and the basophiles. The mature cells which are found in the blood normally, neutrophiles, eosinophiles, and basophiles, arise from their parent cells by a process of ripening.

Fate of the Leucocytes.—Owing to the fact that the leucocytes contain no substance such as the hemoglobin of the erythrocytes, by which their process of destruction may be traced, the ultimate fate of these bodies constitutes a still unsettled problem. The work of Miss Claypole and of Berry tends to show that the spleen is largely concerned in the breaking up of the white corpuscles, but the studies of Ehrlich and Ponfick prove that this organ merely takes up the products of their dissolution. It is probable, therefore, that no particular organ is directly concerned in white corpuscle disintegration, but that they may undergo dissolution in any part of the circulation. Howell asserts that their destruction in the blood stream is a necessary factor for the maintenance of the normal protein content of the plasma.

The Origin of the Platelets and Hemoconia.—Although it is now almost universally agreed that the blood platelets are true formed elements, and not simply concretions or precipitates from the plasma, as was at one time suggested, there is still much diversity of opinion as to their origin. Pouchet's claim that they are extruded from the white corpuscles as polar bodies has been refuted, as have the assertions of Gibson and others to the effect that some of them, at least, arise from the extruded nuclei of the immature erythrocytes. Howell supports the view that the platelets represent the final products of the destruction of the multinuclear leucocytes. In this connection he calls attention to the similarity in size, shape, and staining reaction between the fragmented nuclei of the multinucleated leucocytes and the platelets.

The relatively recent work of J. H. Wright and Dewis presents much reasonable, if not conclusive, evidence as to the origin of the platelets. These observers hold that they are derived from the so-called magacaryocytes or giant-cells of the bone marrow and spleen. Most of these giant-cells are spherical in form, but the property of active ameboid movement which they possess, causes many of them to assume extremely distorted shapes, through the sending out of their cytoplasm in the form of irregular pseudopodia. It is a well-known fact that the giant-cells lose their cytoplasm, and Wright claims that this phenomenon is brought about by the detachment of the pseudopodia in the blood. The fact that the platelets themselves are possessed of ameboid powers upholds this view, and until further light is thrown upon the subject, Wright's theory seems to be the most tenable.

Regarding the source of the hemoconia, at the present time we have no evidence which would justify a contradiction of Müller's original claim as to their origin. It is generally believed, therefore, that the blood-dust represents the débris of disintegrated corpuscles. In particular, the cytoplasmic granules of the leucocytes, especially those of the eosinophiles, are worthy of consideration. For the conclusive solution of this problem much depends upon the discovery of their true chemical composition.

Functions.—To give a full and accurate account of the physiology of the blood would be to enumerate and describe practically all bodily processes. In other words, the normal functioning of all organs and tissues is dependent upon the blood. Even the nervous system, which we have come to regard as being composed of the most highly specialized of all tissues, requires for the carrying on of its work an abundant supply of this fluid. It seems advisable, therefore, in a work of this sort, to speak only of the chief functions of the several constituents of the blood, leaving the reader to apply these same principles to various structures as occasion demands.

The Erythrocytes.—The red corpuscles, if indeed they are cells, are a very highly specialized variety whose sole function appears to be that of carrying oxygen to the tissues from the lungs, and carbon dioxide away from the tissues, which function they perform by virtue of the contained hemoglobin. This important constituent of their make-up forms a

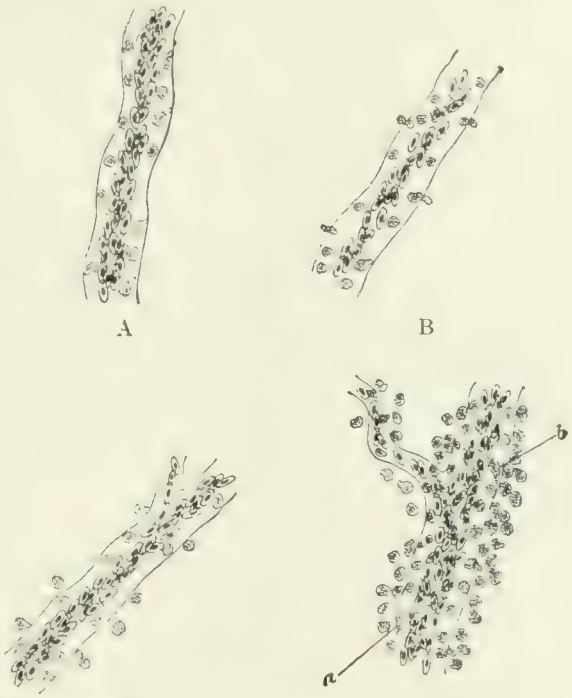


Fig. 699.—A, Leucocytes Sending Forth Processes which Penetrate the Wall of the Vessel. B, Leucocytes partly through vessel wall, showing constriction in center. C, Leucocytes after penetrating wall regain former shape. D, Appearance of vessel and surrounding tissue after diapedesis has gone on for some time. (After Craig.)

very loose chemical combination with one gas independently of its bonds with the other, the two probably uniting with different constituents of the hemoglobin. Both combinations are, according to Bohr, capable of dissociating under suitable conditions of pressure. At any rate, oxygen and carbon dioxide are undoubtedly carried by the corpuscles simultaneously, and there is much evidence to show that the further along the process is continued, that is, the more carbon dioxide the hemoglobin removes from the tissues, the more readily it delivers oxygen. This statement is of course limited by the capacity of hemoglobin to take up both oxygen and carbon dioxide. Setschenow found in the erythrocytes nearly ten per cent. of carbon dioxide, and about five times as much oxygen, which figures give one a good idea of the relative amounts carried.

Loewy suggests that a small percentage of the carbon dioxide in the red corpuscles is carried independently of the hemoglobin, in chemical combination with the alkali.

The Leucocytes.—Perhaps the most interesting property of white blood corpuscles as a class is their ability to make, under certain conditions, ameboid movements—a characteristic which is responsible for the name so often applied to them of "wandering cells." This power is not marked in some of the types, being very much restricted in the lymphocytes, but it is by virtue of this variety of movement that the polymorphonuclears especially are able to perform some of the functions accredited them. For instance, some of them are made to migrate through the walls of blood capillaries, probably between the endothelial plates. The process of migration, known as diapedesis, takes place normally, but is greatly hastened under certain conditions of disease.

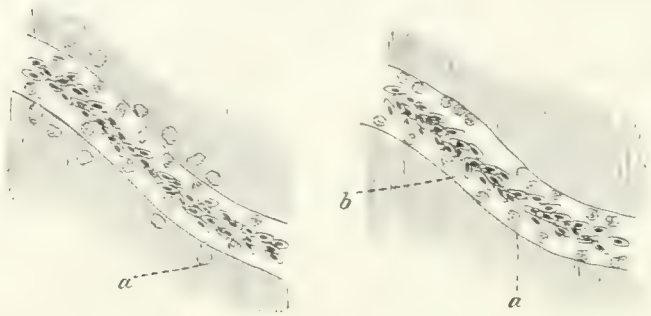


FIG. 700.—A, Small Vein of Mesentery. Showing the arrangement of the granules during and after penetration of wall by the leucocyte. B, Small vein in mesentery. Leucocytes sending off a process clear of granules *a* and *b*. (After Craig.)

It has been discovered that for a maximum degree of activity of the leucocytes a temperature of from 39° C. to 42° C. is required. Movements are very slight, if present at all, below 25° C., and the cells are very quickly killed above 54° C. These observations coincide admirably with our knowledge that the leucocytes show the greatest activity in febrile conditions of moderate intensity in the human body.

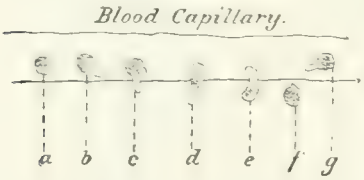


FIG. 701.—Diagrammatic Representation of the Manner in which a Leucocyte Traverses the Wall of a Capillary Blood-vessel. (After Craig.) *a*, Leucocyte before penetrating; *b*, leucocyte sending off process and granules beginning to withdraw to farther end of cell; *c*, leucocyte partly through wall, granules at upper end of cell; *d*, granules passing through the wall; *e*, granules arranged in the portion of the leucocyte farthest from vessel; *f*, leucocyte, after penetration, resuming its original condition; *g*, leucocyte swept from wall, showing retention of the clear penetrating process.

Ameboid movement is accomplished by the sending out of a small portion of the cytoplasm in the form of a pseudopod. Kühne has shown that such an outpushing represents a decrease of the surface tension at the point where it projects, and that this decrease is caused by the absorption of oxygen at that spot, which lowers the cohesion of the molecules. If the object of the cell be that of progression, the whole body of protoplasm gradually flows into the pseudopod, the cell being of approximately the same shape as before, but further on its way by the length of the pseudopod. When, on the other hand, a foreign body is to be engulfed, the pseudopod or pseudopodia, after having surrounded the particle, may be retracted. The surface tension theory accounts for the latter phenomenon by the supposition that oxygen is given off at that point, thus increasing and restoring the surface tension to its original vigor. It does not explain, however, why oxygen happens to be given off or absorbed at these particular points. Some vague chemical attraction is probably the instigating factor.

The power of certain of the leucocytes to ingest, by means of their protoplasmic processes, pathogenic bacteria and other foreign cells or organisms, is the basis of one of their most useful functions, namely, that of *phagocytosis.* As has been suggested, this ability is invested chiefly in the polymorphonuclears and they are termed "phagocytes" or "devouring cells." Metchnikoff believed resistance to bacterial action to be dependent upon the activity of the wandering cells, in mechanically taking up, killing, and digesting bacteria. Wright, however, discovered that the phagocytic power of the leucocytes depends upon the presence of certain serum elements, designated as "opsonins" which sensitize or in some way prepare the bacteria for attack by the leucocytes. He found that it was possible to measure comparatively the amount of opsonins contained in the blood serum of an individual by determining the phagocytic power of leucocytes toward a given bacterium in the presence of the test serum and normal serum. A comparison of the phagocytic indices thus obtained gives the opsonic index, which, associated with contributory clinical signs, to-day serves as one of our most useful laboratory diagnostic tests. As a further step along these lines, Wright found that he could modify the opsonic index of an individual almost at will by the use of vaccines.

Since the study of the internal secretions has reached the point where it is believed that all active cells of the body produce these substances, it has also been suggested that the leucocytes still further, and independently of their phagocytic powers, protect the individual from bacteria by the elaboration of bacteriolysins.

FIG. 702.—Showing a Vessel in Which the Current has Come nearly to a Standstill. The leucocytes are arranged in rows along its wall. (After Craig.)

Beyond their function of protection in local infections, when they emigrate to the point of attack in large numbers, the leucocytes may also, at times, assist in the repair of injured tissues. Covering the necrotic part, and separating it from the adjacent healthy tissue appears a layer of lymph which is largely composed of white corpuscles. When this sequestrated portion is not thrown off, the fluid contained is absorbed, the leucocytes, as well as the dead tissue, may become organized and assist in the development of cicatricial tissue.

Howell credits the leucocytes with helping to maintain the normal protein content of the blood. The blood proteins are of a peculiar nature chemically and are probably not formed directly from the products of digestion. The leucocytes may assist in this process in one or both of two ways. First, by undergoing disintegration in the blood stream, thus con-

ributing their own proteins, and second, by elaborat-ng within themselves substances which maintain he normal composition of the plasma. A suggestive nalogy to the zymogen granules in glandular cells s offered by the formation of granules in the cyto-lasm of the leucocytes.

Observations on the relation between the number f leucocytes in the blood and the elimination of ric acid, led Horbaczewski to advance the supposition hat the purin bodies from the nuclei of disintegrated eucocytes were the chief source of uric acid pro-luction. In conditions where there is an extremely arge number of leucocytes, whether a specific disease, r a leucocytosis produced by the ingestion of drugs,

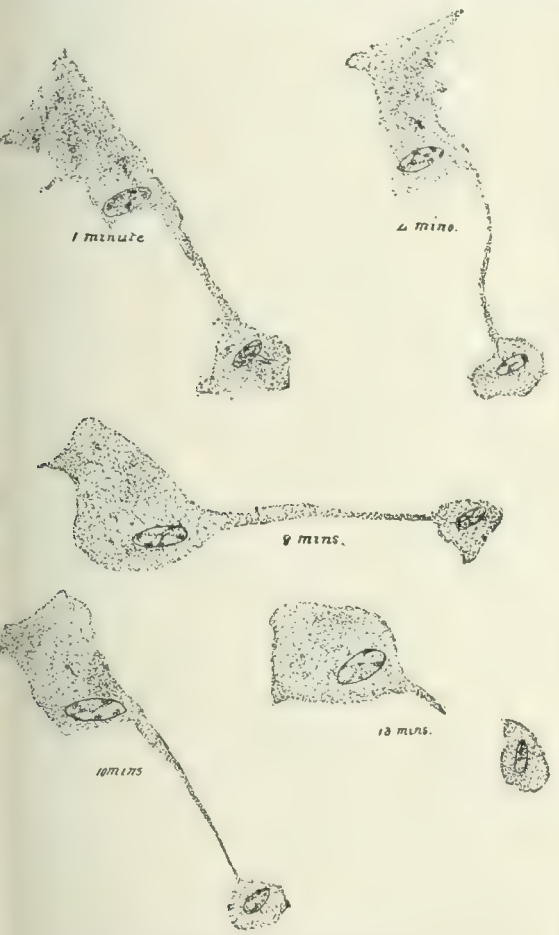


Fig. 703.—Figures of a Leucocyte Undergoing Division (Amphibia). (After Claypole.)

he rate of destruction of leucocytes is proportionately high, and the uric acid elimination correspondingly increased.

Another function of the leucocytes appears to be that of assisting in the absorption of the products of fat and protein digestion in the intestine. It is now generally admitted that the epithelial cells of the gut wall are the important factor in this process, but the leucocytosis of digestion would suggest that the white corpuscles also play a part. They may act either by exerting a chemical attraction for the digestive products or by increasing the selective power of certain of the intestinal cells by means of their internal secretions. These theories apply more particularly to the leucocytes found in the lymphoid tissue of the gut than to the actively circulating cells.

The fats and peptones once within the circulating blood, however, it seems to be a well-established fact that the leucocytes assist in conveying them to the tissue cells. To a certain extent this is brought about directly by diapedesis, but for the most part the nutrient substances are given up to the plasma for terminal distribution by osmosis and filtration. The fact that the leucocytes have been found by Setschenow to contain 2.5 to 3 per cent. by volume of carbon dioxide would indicate that these cells also assist in conveying this gas from the tissues to the lungs, probably in loose chemical combination with the alkali present. Leucocytes or their products are an undoubted factor in the coagulation of blood.

Platelets and Hemoconia.—In view of our limited knowledge of these bodies, little of a definite nature can be said in this section. The original view of Hayem, who believed the platelets to be the precursors of the red corpuscles, is, according to the judgment of most hematologists, untenable. Nearly all modern writers do, however, recognize the close connection of the thrombocytes with coagulation, and Burker and Ducceschi have shown that this process is dependent upon their destruction or solution. The hemoconia, on the other hand, apparently have no relation to fibrin formation, and their function, if any, still remains in doubt.

The Fluid Portion.—The functions of the serum and plasma are described together, for, with the exception of the fibrin-forming substances found in the latter, which have to do with coagulation, a function treated in a separate article, they are identical.

A function of the fluid part of the blood which is of vital importance to the organism is its relation to the equalization of body heat. Various influences, such as friction caused by gross and molecular movement, muscular, glandular, and nervous chemism, combustion of ingested food, condensation of air in the lungs, liquefaction of gases, and the solidification of liquids are constantly at work producing heat within the body. Because of its intimate contact with all body tissues, and the readiness with which it absorbs heat, most of the heat so produced, is given up to the circulating blood. Any of the above factors may have a tendency toward increasing the temperature in one part of the body more than in others, and it is by means of this vigorously circulating fluid that the less active regions are made of a temperature approaching the average of the individual.

We have seen that in the higher animals the average body temperature departs but little from a certain fixed point. In view of the fact that the rate of heat production varies markedly from time to time, according to the activity of the body and the food taken, it is obvious that there is some method of controlling the rate of heat loss. Strictly speaking, the excess is lost by radiation and conduction, dermal and respiratory evaporation, and by means of the feces, urine, and expired air. Furthermore, we must give all due credit to the intricate nervous mechanism of the vasomotor system, for it is by this means that the blood reaches the regions from which heat is lost, in quantities varying with the thermolytic needs of the organism.

It is through the blood, however, and the fluid portion in particular, that all of these methods are made possible, being distributed into complex networks of minute capillaries in the skin and the mucosæ of the lungs and intestines. The total area of exposure of the blood, as represented by the sum of the surface areas of these capillaries, is immense, and affords ample opportunity for the fulfilment of that law of physics governing the equalization of unequal temperatures. In this instance, the air and environmental objects are ordinarily the substances of lower temperature. Hyperpyrexia is brought about by an inability of the vasomotor nerves to compensate for the heat furnished by increased metabolism, rather than by any fault of the blood itself.

While it is true to a great extent that the nervous system is the coordinator of the animal body, we are turning our attention more and more each day to another method which makes use of chemical substances. Comparative physiology shows that as the scale of animal life descends, this method becomes more prominent, the activity and development of the nervous system diminishing in inverse proportion, until in some of the lower forms the chemical method is the only means of unification. The difference between the two methods is essentially one of time, the nervous system being the more rapid by far. These substances have been given the names "hormones" and "colyones" according to whether their functions are those of stimulation or inhibition, but they are all included under the heading of "internal secretions."

The blood serum would seem, in the light of this knowledge to conform to the definition of a coordinator, in that it is the broad highway for the conducting of the internal secretions from their places of origin to the structures in which a specific susceptibility to their action has been developed. It is not intended to deprecate the importance of the nervous system to the body, but it has been shown beyond doubt that it interacts with, and is supplemented by the internal secretions through the blood serum, and that the presence of physiological quantities of these substances in the blood is a necessary factor for the normal functioning of many structures, chief among which are those of the nervous system itself.

Referring again to the protective powers of the blood, it has been discovered that the serum is the most important factor in this respect. Nuttall, Buchner, and others demonstrated that blood serum exhibited definite bactericidal properties; that these properties were more marked in serum free from corpuscles than in whole blood; that the germicidal qualities were destroyed by a half hour's exposure to 55° C. Buchner found that the germicidal bodies were albuminous and that they were active only in weak solutions of certain salts normally found in blood serum. He called these bodies "alexins." They are apparently produced in the tissue cells, are found in greatest absolute amount in serum, but in relatively greater amounts in the blood-making organs. They do not have specific germicidal properties, but tend to prevent infection by any bacterium. They are believed to be responsible for the condition of racial immunity. Inherited immunity against specific bacteria is supposed to arise from the inheritance of ability to produce a specific alexin, in addition to those normally found in the serum. Thus the dog, goat, and others seem to be immune to tuberculosis.

Closely allied to the above, but by a more complex process, is the presence in the serum under certain conditions, of antitoxins, so called because of the power which they possess of neutralizing the toxins of the specific infecting bacterium. This power seems to rest in the globulins of the serum, and is frequently present in such degree that the serum may be used as a therapeutic agent in neutralizing toxins of the same variety in another individual. Antitoxins are of greatest importance in connection with diseases in which diffusible poisons are elaborated by the infecting bacterium, but they do not necessarily possess germicidal properties, nor are they permanent. It is believed that infection with the specific bacterium stimulates the tissue cells to secrete these substances into the blood, where they unite, as does an acid with a base, with the bacterial poisons to form a chemically inert body.

Bacteriolysins are permanent protective bodies developed and poured into the blood serum for the purpose of safeguarding the individual from subsequent attacks by the specific bacterium. They are believed to be responsible for the condition known as acquired immunity, which is found after certain diseases such as typhoid and Asiatic cholera. Upon a later infection, the bacteria lose their motility, become swollen, and soon disintegrate into fine granules which are taken up by the wandering cells.

As a further protective function, the animal organism has the power of secreting into the blood serum, when foreign cells or proteins are injected into it, antibodies which dissolve, precipitate, or otherwise render the harmful substances inert. These antibodies are called "cytolysins," "hemolysins," or "precipitins," according to the substances against which they are specific. Thus, if cow's milk be injected under the skin of a rabbit, there will be produced within the animal's blood, a precipitin capable of precipitating the casein of cow's milk, although it may have no action upon the milk of other animals. In the same way, the injection of spermatozoa causes the production of a cytolysin which destroys this particular form of cell, and the same fact holds good for epithelial cells. Speaking generally, within the serum of any animal hemolysins may be formed that will destroy the blood corpuscles of an animal of another species. But great differences are noted in this respect, the serum of the horse, for instance, showing little hemolytic action upon the red corpuscles of the rabbit when compared with the effect of the serum of a cat or dog. The results of transfusion of blood are, however, so uncertain because of the danger of hemolysis alone, aside from the liability of intravascular clotting, that this operation has largely been discarded. These wonderful protective adaptations of the body are primarily probably chemical reactions dependent upon the properties of the living cells, but the natures of the involved processes are not well understood, and the phenomena are designated provisionally as biological reactions.

In addition to the thrombin, blood serum is said to contain ferments which are capable of converting starch and glycogen into maltose; a cleavage enzyme converting maltose into dextrose; a glycolytic ferment necessary for the combustion of sugar, and a fat-splitting ferment. The extent to which these functions are performed in the blood, however, is uncertain.

Of the twenty-two per cent. by volume of oxygen present in arterial blood, 9.26 per cent. by volume, or, roughly, two-fifths of the total, is carried to the tissues in simple solution in the plasma, according to Pflüger, the remainder, as we have seen, being conveyed almost entirely by the red plastids. Regarding the method of transmission of the carbon dioxide, however, the reverse is true. The results of chemical analyses by various observers show that fully two-thirds of the total carbon dioxide is carried in the fluid portion of the blood. Although it is a fact that the plasma, because of its chemical nature, cannot hold as much of any gas in simple solution as can water, it is nevertheless true that plasma carries much more carbon dioxide than oxygen in this manner. Setschenow claims that fully one-tenth of the total carbon dioxide of the serum is in simple solution. The remainder appears to be in two kinds of union with the components of the plasma—namely, in loose and in firm chemical combination, the designations being made because of the removability of the former portion by means of a vacuum. According to Heidenhain and others, a small proportion is combined with the sodium acid phosphate of the plasma. Another small percentage in undoubtedly held in combination with the serum globulin. But by far the greatest amount of carbon dioxide is joined with those salts to which the alkalinity of the blood is due, that is, with sodium phosphate and sodium carbonate.

The processes by which the two gases enter and leave the blood are those of gaseous osmosis and diffusion, the "animal membrane" involved in the former consisting of the walls of the capillaries plus

the layers of intervening fluid, both within and without. Much the same principles apply to the passage back and forth of nutrient and waste substances other than oxygen and carbon dioxide. Filtration, however, appears to be an additional physical factor in this process. Reference to the section on "Chemistry" will show to a great extent the forms in which these anabolic and catabolic substances are present in the plasma.

General Variations in the Blood.—As a résumé of the general differences existing between arterial and venous blood, the following table is appended:

Arterial Blood.	Venous Blood.
Color.—Bright red, monochroic; oxyhemoglobin.	Purple, dichroic: reduced hemoglobin.
Specific Gravity.—Less.	More.
Number of Corpuscles.—Relatively less; blood more diluted.	Relatively more; blood more concentrated.
Temperature.—Slightly warmer in general.	Slightly cooler, but exceptions; warmest blood in the body found in the hepatic vein.
Coagulation.—More coagulable.	Less coagulable.
Fibrinogen.—More.	Less, except in mesenteric vein.
General Composition.—More uniform.	Numerous local variations.
Gas.—More O, less CO_2.	More CO_2; less O, except in the pulmonary veins.
Water.—More.	Less; transudation of water through the capillaries causes venous blood to be more concentrated.
Urea and Extractives.—Less.	More; except renal vein
Glucose.—More.	Less.
Fat.—Less.	More.
Fibrin.—More.	Less.
Serum Albumin.—Less.	More.
Salts.—More.	Less.

Local Variations of Blood.—Certain organs cause the blood which passes through them to undergo more or less of a modification in respect to its general properties and composition.

The Blood of the Capillaries.—Virchow has noted that the blood from the capillaries does not coagulate after death even when exposed to the air, which apparently indicates some modification of the fibrin or fibrin ferment.

The Blood of the Mesenteric Vein.—More fibrinogen is found in this vein than in arterial blood.

The Blood of the Portal and Hepatic Veins.—Drosdoff has observed in dogs fed with meat, bread, and milk that the portal vein contains fewer corpuscles and more plasma than that of the hepatic. There is also more fatty material present in the portal, which may apparently be stored up in the liver. During digestion the portal vein contains more sugar than the hepatic, but later the reverse is the case, although it is not likely that the portal vein is at any time entirely destitute of it.

The Blood of the Splenic Vein.—The evidence is conflicting here. Some have claimed that a larger number of corpuscles are present in this blood, while others hold that they are fewer and are destroyed in the spleen as well as in the liver.

The Blood of the Renal Vessels.—The differences are best shown in the following table:

	Renal artery.	Renal vein.
Water	790	778
Solids	210	222
	1,000	1,000
Albuminoids	Less.	More.
Mineral salts	More.	Less.
Urea	More.	Less.
Uric acid and creatin	More.	Less.
Oxygen	More.	Less.
Carbon dioxide	More.	Less.

Very briefly, there is loss of water, salts, urea, CO_2, and extractive materials.

The Blood of the Glands.—The blood which leaves a resting gland is dark and possesses the ordinary characters of venous blood; that leaving an active gland is brighter (Bernard) and contains less CO_2 than common venous blood, because a certain amount of the CO_2 is given off in the fluid secreted by the glands, especially the salivary.

The Blood of the Placenta.—This appears to contain more corpuscles and less water than the venous blood of the arms, for example. More urea is also present, but further investigation is necessary.

Menstrual Blood.—Menstrual blood seems to be deficient in the fibrin-forming elements. The blood does not coagulate or only slightly under normal conditions. As this is a capillary hemorrhage and such blood does not coagulate readily, we have a reasonable explanation for this insufficient coagulation phenomenon. Furthermore, the blood becomes mixed with the vaginal mucus and has a tendency toward acidity.

The Blood in Hibernating Animals.—Vierordt has shown that the blood in such animals may show a diminution in the red corpuscles from a total of seven million to two million per cubic millimeter; the changes in the blood with respect to the hemoglobin being very feeble, and but a slight difference existing in general between the arterial and venous blood.

Erle D. Forrest.

Literature.

For the benefit of those readers who may desire more detailed information upon the subject of Blood than has been given in the foregoing pages, as well as for the purpose of acknowledging the valuable assistance which their study has afforded the writer, the works of the following authors may be mentioned among those which have been most frequently consulted in the preparation of this paper: Fish, Dearborn, Howell, Halliburton, Myers, Hammarsten, Abderhalden, Ehrlich and Lazarus, Simon, Wright, Cabot, DaCosta, Buchanan, Türck.

Blood, Circulation of the.—Comparative and Historical Introduction.—All metazoa above the Porifera or sponges possess an internal medium to provide for the nutritive and respiratory needs of those portions of the organism which by their position are excluded from direct relations with the external environment. This internal medium is the blood. In some Cœlenterates it consists simply of water charged with a certain amount of organic particles and occupying the gastrovascular cavity. In higher invertebrates the blood acquires more distinctive properties. Soluble proteins are added conferring coagulability; corpuscular elements appear; and respiratory pigments of some diversity, such as hemoglobin, hemocyanin, or chlorocruorin may be present, belonging as a rule to the plasma rather than to the corpuscles. Invertebrate blood, however, never exhibits the constant chemical composition and independence of the conditions of the external medium which characterizes the blood of vertebrates. Moreover, it is never fully confined to a closed system of definite vessels. The conditions in respect to the latter point show extreme variations. In many of the lower forms there are no proper vessels at all and the blood occupies irregular lacunar spaces of the perivisceral cavity. Highly differentiated types, like Cephalopods and Arthropods, on the contrary, possess a well-developed vascular system comprising a heart, arteries, and veins. There is, however, a more or less complete absence of the capillary connection at the periphery so that in some part or parts of the body, the arteries discharge their contents into the tissue spaces, obliterating the distinction between blood and lymph and leading to the use of such terms as hydrolymph and hemolymph for the blood of these animals.

The term "Circulation" in comparative physiology

is used in the broad sense to describe the motion of the blood. Sometimes this consists merely of an irregular sluggish ebb and flow through tissue spaces and perivisceral cavity resulting from bodily movements. At the other extreme it is a perpetual movement in one direction through a closed vascular system constituting a true circulation in the etymological sense. The more perfect development of the circulatory system in the higher animals is correlated with their more intense metabolic activity, and at the same time acquires important general functions in connection with the regulation of body temperature and the functional coordination of various organs through chemical means, a physiological mechanism whose importance has only recently received adequate recognition. The diagrams of the circulatory systems of the lobster (Fig. 704), the fish (Fig. 705), the frog (Fig. 706), and the mammal (Fig. 707) illustrate some of these essential differences found in the animal series in respect to the organs of circulation. In the crayfish the heart is situated dorsally, surrounded by a so-called pericardium, which is in reality a blood sinus. Six slit-like apertures provided with valves admit the blood during the diastole, and prevent its egress, except by the arteries, during the systole. The arteries ramify minutely but the blood eventually escapes into lacunæ and the perivisceral cavity from which it gradually finds its way to the gills and thence back to the heart. The "arterial" character and dorsal position of the heart and the lack of continuity between arteries and veins are typical for invertebrates. Note the contrast in the circulation of the fish which represents the fundamental vertebrate type. Here the heart is ventral in position, essentially tubular in form, and consists of four consecutive chambers, a sinus venosus, an auricle, a ventricle, and a bulbus arteriosus. The blood is pumped into a ventral aorta which passes forward to supply the gills. The efferent branchial vessels unite to form a dorsal aorta from which all the systemic vessels arise. The arteries are connected with the veins by complete capillary networks and the blood returns to the sinus venosus in a venous condition. The vertebrate heart is primarily a "venous heart."

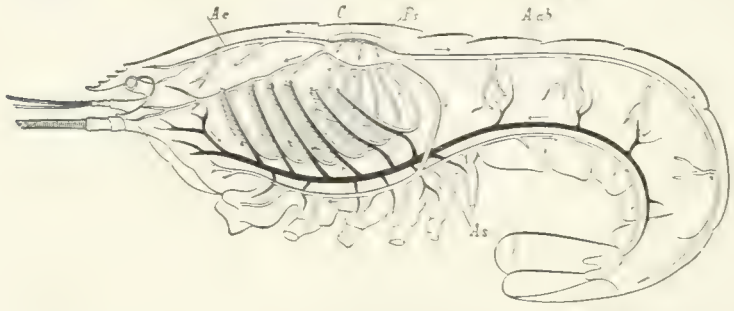


FIG. 704.—Heart, Blood-vessels, and Gills of the Lobster. *C*, Heart in a blood sinus, with *Ps*, several pairs of ostia; *A.ab*, abdominal aorta; *Ac*, cephalic artery; *As*, sternal artery.

In air-breathing vertebrates modifications of this fundamental type are determined by the development of the lungs. The blood-supply of the swimming bladder of the fish is an insignificant part of the systemic circulation. When this organ develops into a lung, its veins establish an independent connection with the heart, and a partition divides the auricle into a right and left half. The ventricle at first remains single as in the frog but complete intermingling of the arterial and venous bloods is prevented by the muscular trabeculæ in the ventricle and the spiral valve in the bulbus arteriosus. The ventricular septum develops gradually in the reptilia, becoming complete in crocodiles as it is also in birds and mammals. In spite of the complete division of the heart in crocodiles, the mixture of venous and arterial bloods is not wholly avoided because of a communication—the foramen of Panizzæ—between the right aorta which arises from the left ventricle and carries arterial blood, and the left aorta with its venous blood.

In birds and mammals only one aortic arch persists and the separation of the two bloods becomes complete. The blood now flows through the vascular system in one constant direction. To make a complete circulation it traverses at least two sets of capillaries, the systemic and the respiratory, as in fishes; but unlike the latter, it also passes twice through the heart. The simple venous heart of the fish is replaced by a double organ with a right venous side which transfers the blood from the systemic veins to the pulmonary artery; and a left arterial side, which returns it again from the pulmonary veins to the aorta. A third set of capillaries may be interpolated in the course of a single circuit. The blood which is distributed to the abdominal viscera is collected by the portal vein and must pass through the capillaries of the liver before returning to the heart. The terms greater or "systemic" circulation, lesser or "pulmonary" circulation and "portal" circulation are commonly used to designate the several subdivisions of the complete path taken by the blood.

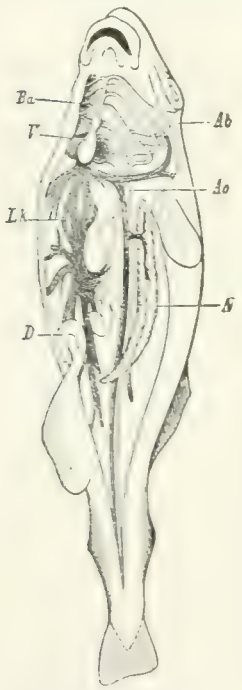


FIG. 705.—Diagram of the Circulatory Organs of an Osseous Fish. *V*, Ventricle; *Ba*, aortic bulb, with the arterial arches which carry the venous blood to the gills; *Ao*, dorsal aorta, into which open the vessels from the gills or branchial veins, *Ab*; *N*, kidney; *D*, alimentary canal. *Lk*, portal circulation.

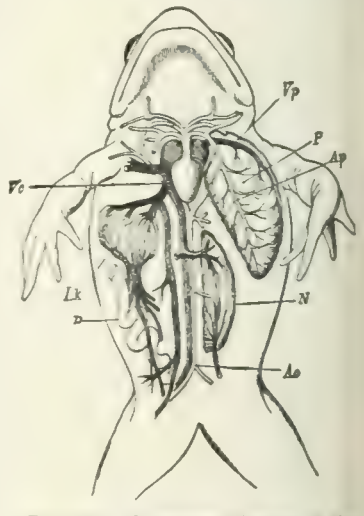


FIG. 706.—Circulatory Organs of the Frog. *P*, Left lung—right lung is removed; *Ap*, pulmonary artery; *Vp*, pulmonary vein; *Vc*, vena cava inferior; *Ao*, dorsal aorta; *N*, kidney; *D*, alimentary canal; *Lk*, portal circulation.

The fact of the circulation of the blood in man was first established by William Harvey in 1616 and his great discovery, aside from the paramount significance of the fact, marks an epoch in the history of medicine in that it was the first example of a

physiological discovery proved by exact experimental methods. Until the middle of the fifteenth century the Galenic teachings were accepted without question. The main features of his physiology so far as the heart and circulation are concerned may be briefly stated as follows: The food absorbed from the alimentary canal is carried by the portal vein to the liver and there converted into blood with certain nutritive properties summed up in the term "Natural Spirits." But this crude blood is unfitted for the higher purposes of the blood in the body. Carried from the liver to the right side of the heart, some of it passes through hypothetical pores of the septum into the left ventricle. Into this same ventricle the heart in diastole draws air from the lungs by way of the pulmonary vein and by the help of its innate heat elaborates "Vital Spirits" which fit the blood for its higher duties. From the right side of the heart the crude blood flows and ebbs to all parts of the body along the veins to serve the lower stages of nutrition. From the left side there is a corresponding flow, followed by an ebb, through the arteries of a purer blood endued with "Vital Spirits," giving to the tissues power to exercise their vital functions. Finally the arterial blood, which reaches the brain, there generates the "Animal Spirits," which pure and unmixed with blood, are carried along the nerves to bring about movements and to carry on the higher functions of the body.

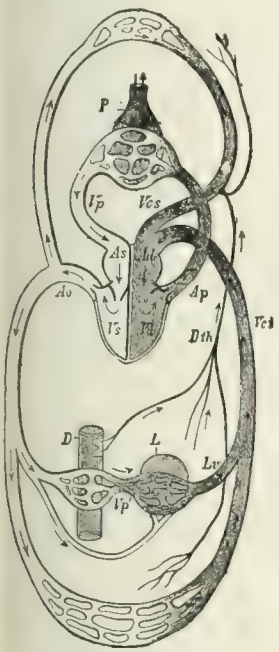


Fig. 707.—Diagram of the Circulation in an Animal with a Completely Separated Right and Left Ventricle and a Double Circulation. (After Huxley.) *Ad*, Right auricle receiving the superior and inferior venæ cavæ, *Vcs* and *Vci*; *Dth*, thoracic duct, the main trunk of the lymphatic system; *Ad*, right auricle; *Vd*, right ventricle; *Ap*, pulmonary artery; *P*, lung; *Vp*, pulmonary vein; *As*, left auricle; *Vs*, left ventricle; *Ao*, aorta; *D*, intestine; *L*, liver; *Vp*, portal vein; *Lv*, hepatic vein.

Harvey had his forerunners in the anatomists of the latter half of the sixteenth century, who undermined the authority of Galen by their demonstration of the impermeability of the interventricular septum (Vesalius, 1555), by discovering the structure of the valves in the veins (Fabricius, 1574), and by significant observations in connection with venesection. A correct account of the passage of the blood from the right ventricle to the left auricle through the pulmonary circuit is found in the writings of Servetus (1553) and Colombo (1559). Indeed it is admitted that Cæsalpinus (1571 and 1593) anticipated correct views in regard to the systemic circulation which were later established on a sound basis by the scientific experiments of Harvey. These earlier statements represent vague and indistinct glimpses of the truth based on anatomical data whose significance was not fully appreciated and whose interpretation was not pushed to a logical conclusion. Harvey began his work with patient and prolonged observations on the living heart until he was able to analyze and describe its complex mechanism; he emphasized the fact that the systole constituted the active phase; that the heart cavities were filled from the veins in diastole and emptied themselves into the arteries during systole. He also studied the blood flow in the vessels,[1] laying especial emphasis on certain quantitative considerations and so proved by irresistible arguments that the blood must move in a circle. His argument throughout is a physical mechanical argument; the question as to immaterial principles, such as heat or spirit, being added to the blood he leaves entirely aside. Once having established the true nature of the circulation, many previously observed facts and phenomena for the first time received a reasonable explanation. The contrary effects of ligatures on the vascularity of a limb, according to their tension, the escape of practically the whole blood by the opening of a single vein, the purpose of the valves in the veins, the details of the structure of the heart, and various phenomena of the body at large both in health and disease found a rational interpretation in the light of the new conception. The old doctrine of the "Spirits" really received its deathblow, though the names survived in the literature for a long time afterward, and the way was opened for the development of true conceptions of the nutrition of the body.

Mechanics of the Circulation.

The closed system of channels through which the blood circulates includes the heart, arteries, capillaries, and veins. The first of these is essentially a muscular force pump whose rhythmical strokes at the rate of about seventy-two per minute drive the blood through the vessels in a constant direction with a considerable velocity. Before taking up the action of the central pump, it will be convenient to note the general features of this blood current.

Its study is essentially a physical problem in hydrodynamics whose complete theoretical treatment is rendered practically impossible by the complex arrangement and mode of branching of the vessels, by the constant change in the physical properties of their walls along their length, and by the continual interaction of their physiological activities. An account of the mechanics of the flow in the vessels must be based mainly on experimental data, and the fundamental laws of hydrodynamics based on the flow of liquids in simple models are introduced merely to assist in the interpretation of these data.

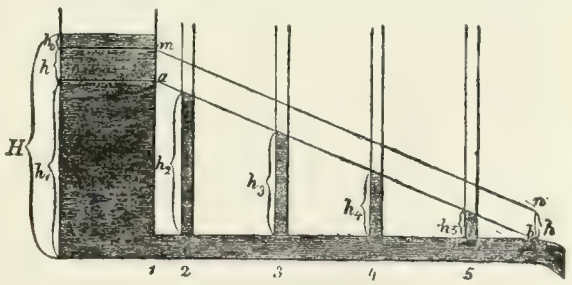


Fig. 708.—Diagram Illustrating the Flow of Liquids in a Horizontal Rigid Tube of Uniform Caliber, when Connected with a Reservoir. (From Rollett.)

The Flow of Liquids in Rigid and Elastic Tubes.—Torricelli's theorem states that when water escapes from an aperture in the side of a reservoir filled to a constant level, the velocity of outflow theoretically is given by the formula $v=\sqrt{2gH}$ in which g equals the acceleration of falling bodies produced by gravity and H equals the height of the column of liquid above the aperture. The actual velocity is obtained by dividing the amount which flows out in a unit of time by the cross-section of the aperture, and experiment shows that this is less than the theoretical value. A

part of the energy of position represented by the column of liquid H is lost at the aperture through the mutual interference of the particles of water as they approach the opening from different directions, the result of which is the so-called "contractio venæ" near the beginning of the jet. If the lost fraction of the total energy be represented by a column of liquid equal to h_o and the energy spent in giving velocity by h, then the total height $H = h_o + h$. Now suppose a horizontal rigid tube of some length attached to the aperture in the reservoir (see Fig. 708). The velocity of outflow from the end of the tube can again be calculated from the volume of outflow and the cross-section of the tube; then by substituting this value of v in the formula $v = \sqrt{2gH}$ it will be found that h, the portion of the total energy of position H that is available for velocity, is less than in the case of the free aperture. A second portion of H has been consumed in overcoming the resistance in the tube. Call this part h_r, then $H = h + h_o + h_r$.

When liquids wet the sides of the tube through which they flow, the layer of particles next the wall of the tube may be considered practically at rest on account of adhesion. The layer next within moves along slowly, the next a little faster, etc., the velocity increasing with each successive layer to the axis of the tube, where it reaches a maximum. By the velocity of the whole stream as calculated for the tube above is meant the mean or average velocity of all the layers, and it has been shown that when the bore of the tube falls within certain limits so that the movement of each particle of liquid is parallel to the axis, this mean velocity equals one-half the axial or maximal velocity.

The resistance to the flow of liquids in tubes thus appears as a case of internal friction, as if the whole column of liquid were made up of a series of concentric cylinders, each moving a little faster than the next larger, and the outermost one completely at rest against the sides of the tube. This internal friction constitutes a resistance which retards the flow and puts the liquid under tension felt as lateral pressure against the walls. Gages arranged along the tube (h_2, h_3, h_4, h_5, Fig. 708) to indicate this pressure show that at each point it is proportional to the amount of resistance beyond and that it becomes zero at the free outlet. In tubes of uniform caliber the lateral pressure drops uniformly; but where narrower and wider sections alternate, the fall is irregular for obvious reasons. Liquids being incompressible, the amount of fluid passing each cross-section anywhere along the tube in a second must be the same; the rate of flow, therefore, at each point will be inversely proportional to the width of the tube. The more rapid flow and consequent increase of internal friction in the narrow portions make heavier draughts on the store of available energy, and the lateral pressure falls more quickly here than in the wider portion.

In a system of tubes like the blood-vessels, in which the main channel subdivides dichotomously into numerous smaller branches whose total sectional area far exceeds that of the original trunk and in which these branches are gathered again into a single large trunk the velocity is determined by the same law of inverse proportion to the width of the bed, and is therefore slowest in the smaller tubes where the total area is greatest. On account of the slowness of the current, the pressure should fall slowly in this region; but the increase of surface in the numerous narrow channels operates the other way, so that the actual rate of fall in the pressure will depend on the relative magnitudes of these two opposing factors.

As regards the nature of the tubes, the same laws apply with equal force, whether the walls are rigid or elastic, provided only the flow is continuous and uniform. When instead of the steady continuous pressure of a column of liquid, an intermittent force is used to drive the liquid into the tube, the character of the wall makes its influence felt. The capacity of a rigid tube being invariable, the inflow and outflow must be synchronous and equal in amount; an intermittent charge necessarily implies an intermittent discharge. An elastic tube when short and wide behaves in the same way; but if from increase of length or constriction at the outlet resistance arises, the outflow no longer corresponds in time to the inflow. The injected liquid is partly retained by the tube, whose walls yield to the distending force of the lateral pressure, and is discharged only in the succeeding interval by their elastic recoil.

If the intermittent influx is rhythmically repeated at sufficiently short intervals, each new charge arriving before the previous one has been displaced, the outflow becomes continuous. By properly adjusting the resistance in the tube to the force, rate, and stroke of the pump, an elastic tube can be made to convert a rhythmical intermittent current into a continuous even stream.

The Blood Flow in the Vessels.—1. *General Account of the Vascular System.*—The arteries and veins physiologically are merely conducting channels to and from the capillaries, which alone are fitted by the structure of their walls to bring the blood into nutritive relation with the tissues and enable it to fulfill the function of an internal medium. The arteries possess stout walls which are both elastic and contractile. Their elasticity is slight but perfect, yielding readily to a distending force, but returning to their original size as soon as the distending force is removed (Fig. 709). At zero pressure the

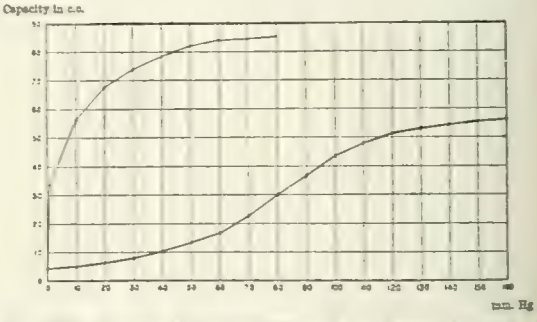


Fig. 709.—Curves of Distensibility of an Artery (thick line) and of a Vein (thin line). The figures at the left side of the diagram represent the capacity of a section of the vessel when distended under a certain pressure, expressed by the figures on the base line in millimeters of mercury. (Starling.)

artery does not completely collapse. With rising pressure the distention is small at first, becomes more rapid between the limits corresponding to physiological variations of blood pressure, and then with each additional rise of pressure shows a gradually diminishing increment. The result is that the distention of the arteries under the influence of a rising blood pressure soon approaches the point where any further increase of size requires a disproportionately great rise of pressure. The cohesion of the vessel walls is also considerable and capable of withstanding many times the strain normally put upon them in the body. The carotid of sheep, for example, is ruptured only when fourteen times the usual pressure it is called upon to bear is put upon it, and the human carotid resists a pressure of eight atmospheres. The relative proportion of muscular and elastic tissue varies in different arteries, the elastic tissue predominating in the large arteries near the heart, while the smaller ones near the periphery are eminently muscular and contractile. It appears from the data available up to this time that for a given rise of pressure the distensibility of the arteries increases with their distance from

the heart. By their elasticity the arteries convert the intermittent discharges of the heart into a continuous and steady flow in the capillaries and by their contractility they regulate the distribution of the blood according to the needs of the several organs. As they leave the heart the arteries continually break up into smaller branches until they terminate in the capillaries. At each point of bifurcation the resulting branches individually are smaller than the parent vessel, but taken together their area is greater. Hence the sectional area of the arterial bed increases steadily toward the capillaries, the total cross-section of which is several hundred times that of the aorta (Fig. 710).

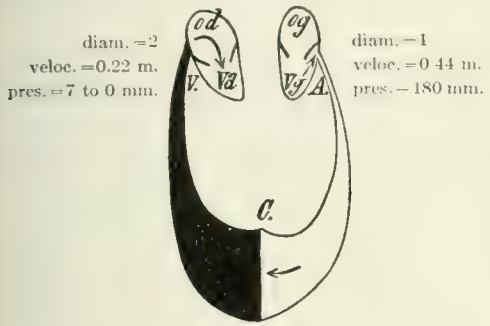


Fig. 710.—Schema of the Major Circulation. *A*, Arterial cone; *V*, venous cone; *C*, capillary expanse.

The capillaries with their delicate endothelial walls are elastic, and yield readily to changes of internal pressure. This alone would account for the observed variation in the size of their lumen within the wide limits of 5 to 20μ; but in addition they are believed to possess the power of active contractility.

The veins have thin walls in which white fibrous tissue predominates, but in which some elastic and muscular elements also occur. Their curve of extensibility shows that their capacity, which is nothing at zero pressure increases rapidly at first on raising the pressure, but quickly reaches the limit of extensibility. Their cohesion is even greater than that of the arteries. Given a vein and an artery of the same thickness, a greater force is required to rupture the former than the latter. The elasticity and contractility of the veins serve mainly to adapt the capacity of the whole vascular system to variations in the quantity of blood, and thus to regulate the filling of the heart in diastole. The cross-section of the bed again diminishes in the veins in passing from the capillaries to the heart; but since the venæ cavæ together have nearly twice the area of the aorta, the total capacity of the veins far exceeds that of the arteries. The veins, in fact, can easily hold the total blood of the body, as is practically the case after death when the arteries are empty, and in the paradoxical experiment of bleeding an animal to death into its own veins.

2. *The Blood Pressure.*—Familiar experiences of daily life have long since made some of the differences between the character of the current in the arteries and in the veins a matter of common knowledge. The arteries present to the finger a sense of resistance which increases rhythmically at each heart beat and expands their walls, producing the so-called "pulse." When an artery is severed, the blood spurts from its central end with considerable force, the jet being continuous but not equable. Finally when an artery is ligated, it swells on the proximal side while on the distal side the pulse disappears and its walls collapse. Compare with all this the behavior of the veins; they are soft and easily compressed; there is no pulse; the blood issues in a gentle continuous stream from the distal cut end, and a ligature distends them on the peripheral side. These facts demonstrate a difference not only in the direction of the current in the two kinds of vessels but also in the tension or internal pressure.

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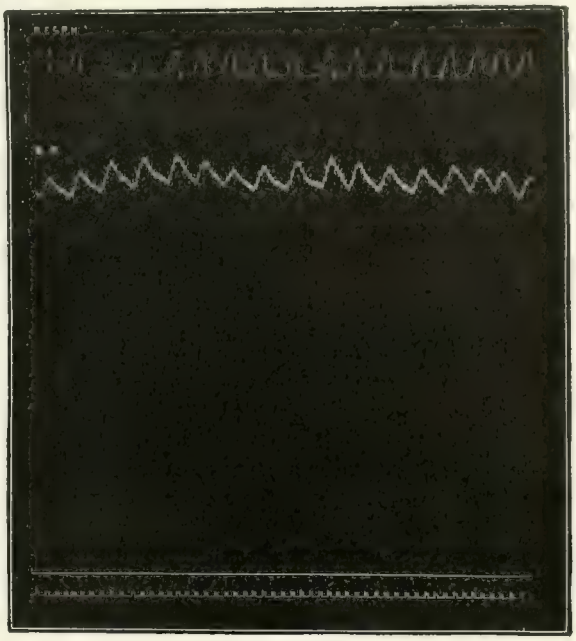

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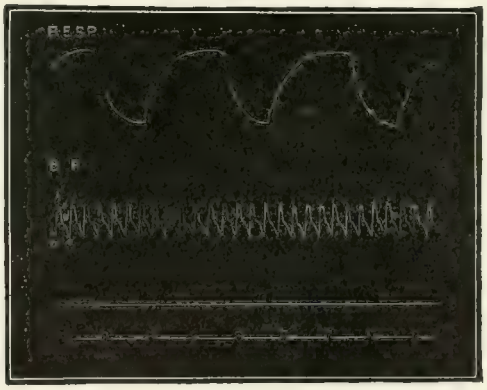

Fig. 711, A.—Tracing of the Blood Pressure from a Rabbit Taken by the Mercury Manometer. *B.P.*, Curve of blood pressure. The horizontal line at the base shows the position of the zero pressure. Time tracing in seconds. B.—Normal blood-pressure record taken from the rabbit with a Hürthle manometer. The horizontal line again shows the position of the zero pressure. Time in seconds.

Stephan Hales first measured the pressure in the arteries of living animals (1773). His method was to connect the central end of an artery with a vertical tube and to read off the height to which the blood rose. Owing to the error from loss of blood and to inconvenience from frequent clotting in the tube, the original method is not suited for prolonged and accurate observations. The mercury manometer was substituted by Poiseuille (1828) to meet these

difficulties, and this instrument, with a float and writing style added, marks the beginning of the use of the graphic method in physiology. The mercury manometer satisfies the requirements in all cases involving questions of mean blood pressure and

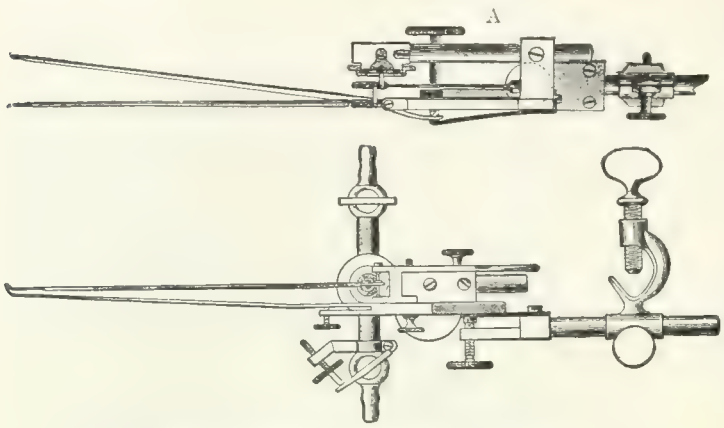

FIG. 712.—*A* and *B*, Hurthle Spring Manometer.

remains in general use for this purpose. On account of its great inertia, however, it cannot record with accuracy sudden and extensive variations like those produced by the systole and diastole of the heart. Various forms of spring manometers have been devised to register these changes of pressure, some of them having developed the capacity of responding accurately to a change of 10,000 millimeters of mercury per second (Fig. 712).

These methods are rarely applicable to man as they require vivisection. Special devices had to be invented to obtain records of the blood pressure in human beings, since the practical importance of even approximate data regarding blood-pressure

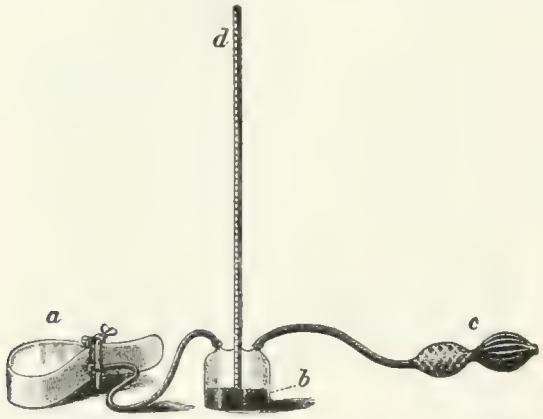

FIG. 713.—Sphygmomanometer of Riva-Rocci. (Sahli.)

variations in health and disease has been recognized. The principles on which these clinical methods are based were suggested by von Basch (1887) and Marey, and a number of instruments, known in general as sphygmomanometers, have been devised for their practical application. It must be remembered that the blood pressure in the arteries oscillates between a maximum or "systolic" and a minimum or "diastolic" pressure in each cardiac cycle. The principle of von Basch consists in determining the amount of pressure required to obliterate the lumen of the artery and so extinguish the pulse beyond the region of compression. The best-known instrument based on this simple principle is the Riva-Rocci sphygmomanometer (Fig. 713). It measures only the systolic arterial pressure. The measurement of the diastolic pressure is based on a principle suggested by Marey and first applied by Mosso. The method consists in finding the external pressure under which an artery shows maximal pulsations; this pressure is equal to the diastolic pressure.

The Erlanger apparatus (Fig. 714) combines the von Basch and Marey principles in a practical form for both systolic and diastolic blood-pressure determinations. Convenient forms of apparatus applying this principle have also been devised by Hill, Mosso (Fig. 715) and others.

Direct measurement by one or another of the methods enumerated above shows that the mean blood pressure throughout the arteries is high, being greatest in the aorta, and falling steadily but slowly toward the capillaries. For example, aortic pressure in the dog, 130 to 180 mm. Hg.; rabbit, 100 to 130 mm.; horse, 150 to 200 mm.

In man the aortic pressure cannot be determined directly; but in view of the comparatively small differences among mammals of all sizes, it is usually assumed to be about 150 mm. Hg., an estimate consistent with re-

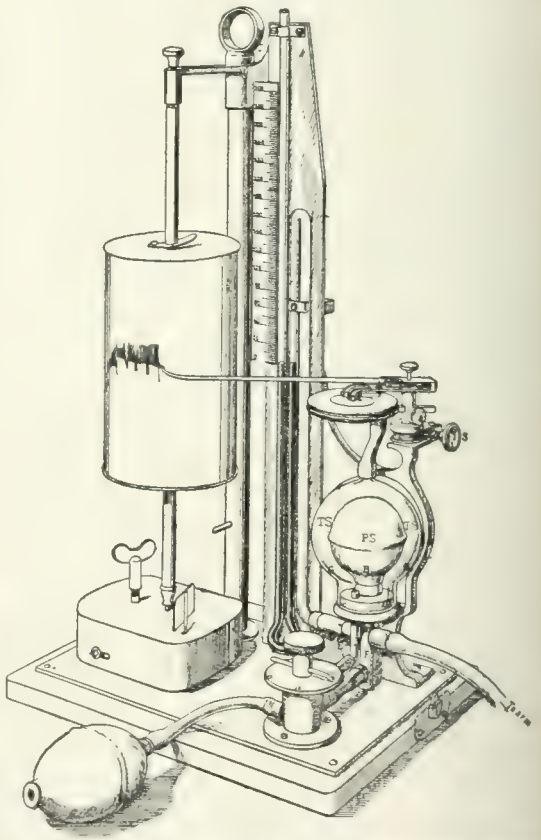

FIG. 714.—The Erlanger Apparatus. (Johns Hopkins Hospital Reports, Vol. xii., 1904.)

sults obtained on peripheral arteries by various observers. Thus Albert found the pressure in the tibial artery of a boy, 100–160; von Basch, in the radial of man, 135–165; Faivre, in the brachial of

man, 110–120; Hill, in the brachial of man, 100–120; and Mosso, in the digital artery of man, 100.

The pressure in the arteries shows, moreover, rhythmical oscillations synchronous with the systole of the heart. The mercury manometer does not register these rapid changes with any accuracy on account of its great inertia. Their relative extent as compared with the mean blood pressure was recognized only after the introduction of spring manometers. Thus in the aorta of a rabbit Hürthle found the difference between diastolic and systolic

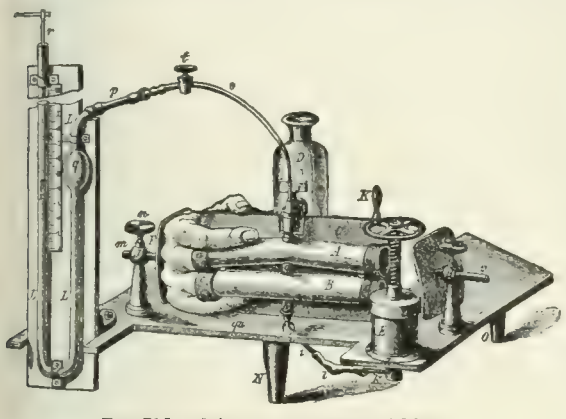

Fig. 715.—Sphygmomanometer of Mosso.

pressure to equal 40 to 50 mm. Hg., *i.e.* about one-third the total mean pressure. This difference between the systolic and the diastolic pressures is known as the "pulse pressure." It is greatest in the large arteries, becomes less in the smaller arteries at a distance from the heart, and disappears altogether in the capillaries and veins under normal conditions.

Second, the mean pressure is low in the veins throughout, but higher in the small veins, gradually becoming less toward the heart; in the external jugular and similar vessels close to the heart it may even fall below zero.

Thus, in the sheep the following figures have been obtained: Pressure in the external facial vein, 3 mm. Hg.; pressure in the brachial, 4 mm. Hg.; branches of brachial, 9 mm. Hg.; crural vein, 11.4 mm. Hg.

The pressure in the capillaries must be determined by indirect methods. Valuable indications of changes of pressure within them are gained from simultaneous records of the pressures in the corresponding artery and vein. To obtain a measure of the absolute capillary pressure von Kries applied pressure to the skin or mucous surface and determined the weight necessary to produce a visible change of color (blanching), which was taken to mean collapse of the capillaries. The result, which he places at 33 mm. Hg. for the rabbit's gum, is regarded as a rough approximation, but it is sufficient to indicate that the capillary pressure is intermediate between that of the arteries and of the veins respectively.

There is consequently a continuous though irregular decline of pressure from the aorta to the right auricle. The fall is slow and gradual in the arteries and veins, but between the small arteries and small veins, *i.e.* in the region of the arterioles, capillaries, and venules, it is marked and sudden. The curve of pressure would, therefore, have some such form as that represented in Fig. 716.

The circulation in the peripheral region, where the greatest changes obviously take place, can be directly observed in transparent organs with a microscope. The blood is there seen to pass in a continuous stream from the small arteries through the capillaries, to the veins. The velocity is greater in the arteries than in the veins, and greater in both than in the capillaries. Faint pulsations synchronous with the heart's beat are also visible in the arteries, but these disappear in the capillaries and veins. In the small capillaries the corpuscles are pressed through in single file and occupy the whole bore, but in larger capillaries, and especially in the small arteries and veins which permit the passage of more than one corpuscle abreast, the red corpuscles run in the middle of the channel, forming a red core, while a colorless layer of transparent plasma is left between it and the sides of the vessel. These are known respectively as the "axial current" and the "inert layer," "peripheral zone," or "Poiseuille's space." In the plasmatic layer white corpuscles are frequently seen clinging to the sides of the vessel, sometimes rolling slowly along, and in general having an irregular motion with frequent temporary stops. In all cases the blood as it passes through the capillary stretches and expands the walls, and the flow is subject to many variations. Rarely are the capillaries equally distended throughout a given field, and frequently the corpuscles will appear to remain stationary in one or more of them for a brief period and then to move on again. The whole picture manifestly shows that the passage through the capillaries is attended with considerable difficulty. The resistance to the flow of the blood caused by friction is small in the large arteries; it increases gradually as they divide, but receives its chief and most important addition in the minute arteries and capillaries, especially in the former, on account of the flow being more rapid in them. This constitutes what is so frequently referred to as the "peripheral resistance" and is one of the most important physical factors in explaining the circulation.

The high pressure and pulsatile flow in the arteries, the steady stream through the capillaries, and the low pressure and uniform flow in the veins can all be explained on purely physical principles. In the systole of the ventricle (1), driving a certain quantity of blood into the aorta at regular intervals and with a certain force; the long stretch of elastic branching arteries (2), and the peripheral resistance (3) are provided all the conditions which were shown above to be necessary for the conversion of an intermittent into

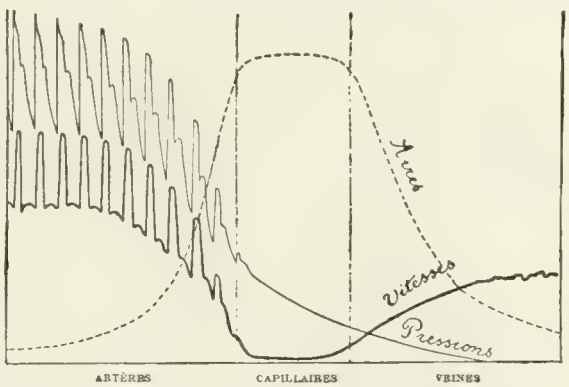

Fig. 716.—Schematic Representation of the Variations of Pressure, Velocity, and Sectional Area of the Different Parts of the Circulatory System. (Modified from Gad.)

a continuous current, while the veins afford a free and easy passage for the blood back to the heart when the greater part of the energy imparted by it to the blood has been expended in passing the peripheral resistance. The circulation in the vessels at any moment represents a state of dynamic equilibrium which is subject to constant variations. The energy of the heart's action may be altered by variations in the rate, volume, and force of its strokes. Again, the peripheral resistance may vary in con-

sequence of changes in the caliber of the vessels. Constriction on their part over any considerable area will raise, widespread dilatation will lower, general arterial pressure. Changes in both heart and arteries are constantly taking place, and indeed are necessary and essential. A fixed and rigid condition of the circulatory apparatus, devoid of adjustments within wide limits to adapt the blood flow to the varying needs of the several organs, would be worse than useless; it would be positively harmful. The mechanisms by which these changes are effected will be considered below. A third factor which may exert some influence on the blood pressure is the quantity of blood contained in the vessels. The amount normally present would be able with the heart at rest to produce a uniform mean pressure of only 5 to 10 mm. Hg. throughout the vascular system in dogs. But during life the heart maintains a continuous circulation by accumulating the blood in the arteries under a positive pressure, thanks to the peripheral resistance and elasticity of their walls, while the veins are emptied to a corresponding extent and the pressure within them reduced below the mean. Experimental investigation of the effect of increasing or diminishing the quantity of the circulating medium has shown that variations in both directions and within considerable limits have a surprisingly little effect on the arterial pressure, compensating mechanisms being provided for quickly restoring it to, and preserving it at, the normal level. These mechanisms are manifold and complex as shown in the following illustrations. In case of copious intravenous injections, say of defibrinated blood or normal saline solution, producing a state of hydremic plethora, the increased volume of blood is first provided for by relaxation and dilatation of the vessels. The veins especially expand to accommodate the increasing mass and in extreme cases their overdistention may be plainly seen and the liver becomes hard to the touch. By this relaxation of the vessels and because of the less efficient ventricular systoles due to overdistention of the heart, the arterial blood pressure tends to remain at or near the normal. The capillary pressure on the contrary is raised and this brings into play other mechanisms by which permanent relief is secured. Transudation into the tissues removes a part of the injected fluid from the vessels, while the secretory activity of the kidneys and intestinal mucosa is enormously heightened and thus disposes of another portion. The character of the injection naturally exercises a decided influence on the relative share of these several mechanisms in the total result. In the case of hemorrhage the reverse series of changes are noted. There is a more complete emptying of the heart at each systole, a general contraction of the vessels, a restricted secretion from the kidneys, salivary and other glands, and a rapid absorption of lymph into the vascular system. In conclusion, two general facts in regard to the blood pressure deserve special mention: First, its remarkable constancy under ordinary circumstances in spite of many modifying influences; second, the important and extensive variations, seemingly out of all proportion to the exciting causes, occasionally produced by trifling and insignificant stimuli.

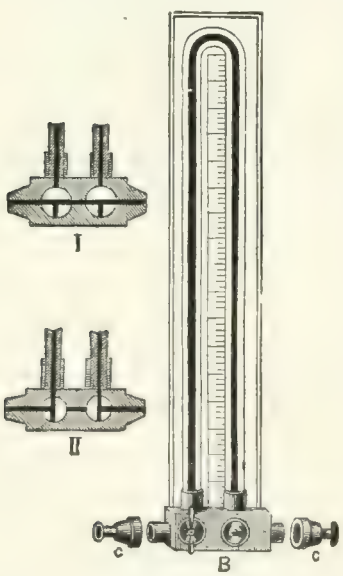

Fig. 717.—Volkmann's Hemodromometer. I, Blood flows from artery to artery; II, blood must pass through the glass tube of *B*; *c*, *c*, cannulæ for the divided artery.

3. *Velocity of the Blood Current.*—In considering the rate of flow in the vessels it is important to distinguish between the average velocity for a given period of time and the actual velocity which constantly oscillates above and below this mean with every phase of the heart's beat and with every variation of the peripheral resistance. Volkmann first measured the mean velocity in the arteries in 1846 with his hemodromometer (Fig. 717).

The principle of the method is simply to determine the volume of blood flowing through an artery in a given period and dividing by its cross-section. The quotient represents the length of a cylindrical column of blood with a base equal to that cross-section, and therefore measures the average velocity in that time. Ludwig afterward devised a more convenient instrument, the stromuhr or rheometer (Fig. 718) by means of which numerous data have been collected. The results are not entirely exact, on account of inherent imperfections in the method, but they may be regarded as approximately true. Even in the course of a single experiment the mean velocity in the carotid or other large artery is found to vary considerably for reasons which will be stated presently. Disregarding these variations for the moment, the rate of flow in the carotid of the dog or horse, and probably also of man, may be placed at from 300 to 500 millimeters per second. The rate diminishes in the smaller arteries the further one goes out from the heart, and becomes slowest in the capillaries. As measured in the web of a frog's foot under the microscope, it is about 0.5 millimeters per second. There are reasons for supposing it somewhat greater in the capillaries of mammalia, where it has been estimated at about 0.8 millimeters per second. On leaving the capillaries the flow is quite slow in the venous radicles emerging from them, but it increases as these join into larger trunks, until finally it attains a velocity approximately equal to one-half that with which it started in the aorta. These changes in the mean velocity along the system are determined according to one of the simple laws of hydrodynamics stated in the preceding section. A continuous circulation in a closed system implies that an equal quantity of fluid passes each cross-section in a given time. Now the quantity which passes may be expressed as the product of the velocity by the cross-section, thus $Q = V \times A$. And similarly $Q' = V' \times A'$, etc. But Q, Q', etc., being equal to one another $V \times A = V' \times A'$, hence $V : V' :: A' : A$, or the velocity varies inversely as the cross-section along the system.

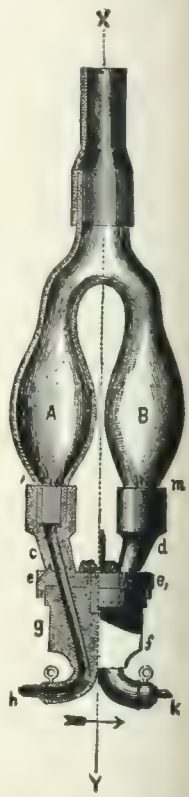

Fig. 718.—Ludwig and Dogiel's Rheometer. *X*, *Y*, Axis of rotation; *A*, *B*, glass bulbs; *h*, *k*, cannulæ inserted in the divided artery, *e*, *e*, rotates on *g*, *f*; *c*, *d*, tubes.

It was stated above that the arterial tree widens

out steadily from the aorta to the capillaries (see Fig. 710). Comparison of the respective velocities at these two points now shows that the amount of this increase must be something like 500 times. For a graphic representation of the relative velocities throughout the vascular system and their relation to the sectional area, see Fig. 716 above. This dependence of the velocity on the width of the bed applies of course only to the general rate of the whole system, and many local and transient variations, constantly occur. Since the real cause of the flow from one point to another is the difference of pressure between those points, the actual velocity at each moment must depend on the amount of this difference of pressure and the resistance against which it is working. A change in either of these factors will necessarily affect the local velocity. An illustration of this is found in the following observations on the rate of flow in the carotid of the dog by Dogiel:

Weight in kilograms.	Period of observation, in seconds.	Rate of flow in millimeters, varied.
23.3	80	From 733 to 349
12.1	127	From 520 to 243
3.2	63	From 458 to 411
3.6	45	From 339 to 204

The slowing of the current observed in each case is not referable to incipient coagulation or other experimental error, at least not to any great extent; on the contrary, it is due to changes in the condition of the peripheral area supplied by the carotid artery. Blood pressure remaining the same, the rate of flow becomes essentially a function of the peripheral resistance. The temporary interference with the circulation during the adjustment of the instrument destroys the tone of the vessels beyond, and lowers the resistance, so that the observed rate is at first too high. With circulation reestablished the normal caliber is regained, the resistance increases, and a corresponding retardation is observed.

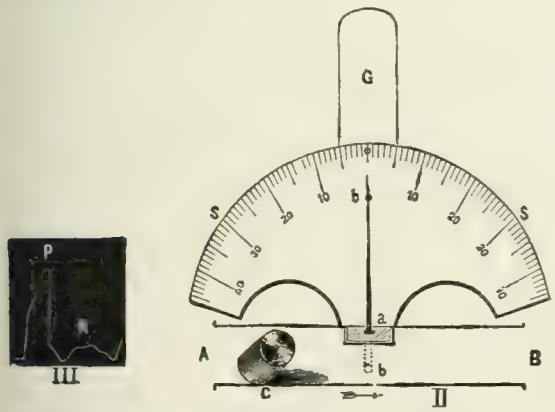

Fig. 719.—II, Dromograph. *A*, *B*, Tube inserted in the artery; *C*, lateral tube connected with a manometer; *b*, index moving in a rubber membrance, *a*; *G*, handle. III, Curve obtained by dromograph.

It will be noticed that this quickening influence of a local dilatation is in no sense a contradiction to the general principle that the rate of flow is inversely proportional to the width of the bed. The local change is not extensive enough to affect the total cross-section of that level appreciably, but by reducing the resistance along one of numerous alternative paths increases the flow in that direction at the expense of the others. In such cases the flow of blood through the widened artery or arteries is for the time being increased in rapidity, not only in spite of, but actually in consequence of the artery being widened. The influence of changes in the blood pressure on the velocity is shown in the effect produced on the latter by each beat of the heart. When the velocity of the flow is recorded by means of an instrument which will register its finer variations, say with the hemodromograph of Chauveau and Lortet (Fig. 719) at the same time that a pressure curve is taken with a spring manometer, the result shown in (Fig. 720) will be obtained.

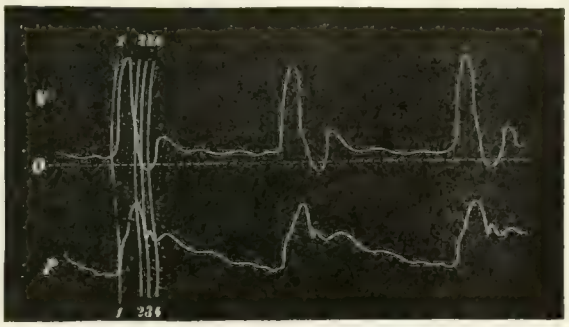

Fig. 720.—Curves of Velocity (*V*) and Pressure (*P*) from the Carotid of the Horse. (According to Lortet.) The lines 1, 2, 3, 4 mark corresponding points in the two curves. The ventricular systole begins at 1; the diastole begins somewhere between 3 and 4.

The record shows a marked acceleration during cardiac systole, the rate in the carotid of the horse rising to 520 millimeters per second as compared with 150 millimeters during diastole; and, indeed, the difference may be even greater than this after a general vasodilatation such as that following section of the spinal cord, when the diastolic rate falls extremely low.

The variations in the rate of flow in the arteries can be measured in man by an indirect method. When the volume of the arm is recorded by means of a plethysmograph (Fig. 721), the changes which are observed are due to variations in the size of the arteries and indicate corresponding variations in the rate at which the blood enters them, the outflow from the veins being uniform. From the volume curve (see Fig. 722) Fick constructed the curve of velocity, and found that it resembles closely the curve of Lortet obtained by the direct method on the horse.

4. *The Circulation in the Veins.*—This is influenced by a number of accessory factors, whose combined effect renders it somewhat irregular perhaps, but which on the whole promotes and quickens it. Among these secondary helps to the circulation the following are usually included, although the fact must not be lost sight of that the real cause of the venous flow is the ventricular stroke, enough of whose energy remains, after driving the blood past the peripheral resistance, to carry it along the veins back to the heart.

(*a*) Aspiration of the Thorax.—It has been stated above that the pressure in the great veins near the heart sinks below zero or atmospheric pressure. This is due to their position in the thorax where a permanent negative pressure prevails. With each inspiratory movement this negative pressure is increased while abdominal pressure is raised. The blood in the large veins of the neck, upper extremities, and abdomen is forced or sucked into the thoracic veins and right auricle by these altered pressure relations. In expiration, the reverse changes in pressure occur, but the valves in the jugular, subclavian, and other veins prevent a reflux and so the

net result of the respiratory movements is to promote the circulation in the veins.

(*b*) Contraction of the Skeletal Muscles.—Many of the veins possess valves which open freely toward the heart but effectually block the passage of the blood in the opposite direction. External pressure on such veins forces their contents along toward the heart while they fill again from the peripheral end when the pressure is removed. Something of this sort occurs in all bodily movements in which the muscles by their alternate contraction and relaxation provide the intermittent compression. The pumping action of the muscular movements is an important factor in maintaining the circulation in the lower extremities where the hydrostatic pressure opposes the return of the venous bood. It also plays an important rôle in the stomach and intestines during digestion periods by its effect on the circulation in both veins and lacteals. Similarly the musculature of the spleen is supposed to aid the circulation through that organ by its rhythmical contraction. It has been suggested that the pulsation of the arteries may exercise a feeble mechanical effect by their rhythmical shocks against the closely applied venæ comites.

(*c*) Posture.—Mere changes in the position of the limbs and body may affect the pressure in the veins by altering the tension of their walls (Braune). Thus in walking, the femoral vein where it passes under Poupart's ligament collapses when the leg is rotated backward and outward, but fills again when the leg returns to its first position, the whole movement making a kind of suction and pressure apparatus.

(*d*) Gravity.—In the upright position of the body, the difference of hydrostatic pressure in the vessels of the head and feet amounts to 1.75 meters of water or 129 millimeters of mercury. Gravity

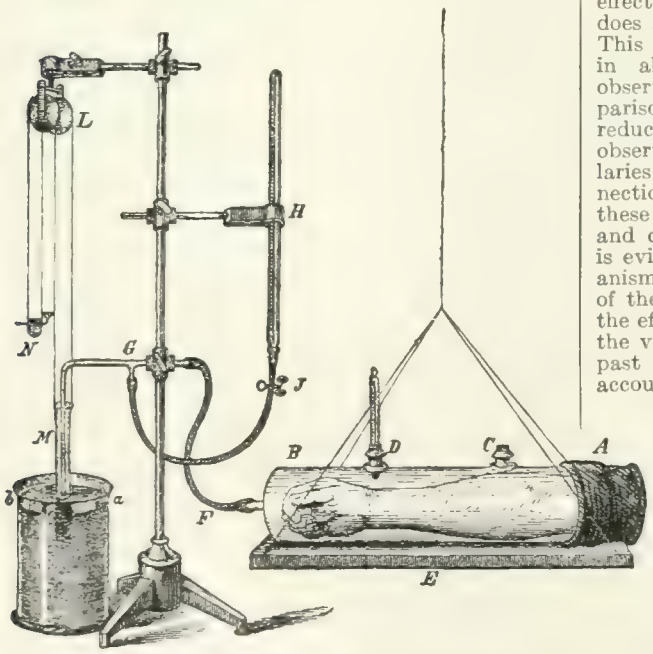

Fig. 721.—Plethysmograph. (According to Mosso.)

evidently opposes an upward current and assists a downward one, so that the effect on the arteries and veins to any part is equal but opposite in direction. This influence modifies the distribution rather than the rate of flow of the blood, as may be seen on comparing the pale anemic condition of the hand raised above the head with its congested appearance when hanging at the side. The hydrostatic effect under normal conditions is compensated by contraction of the arterioles and of the abdominal walls, thus preventing the stagnation of the blood in dependant parts and in the great splanchnic area. In the case of rabbits which have lax abdominal walls, it is possible to kill the animal by simply holding it vertically for some time. In man the compensating nervous reflexes may be lost or weakened, as in

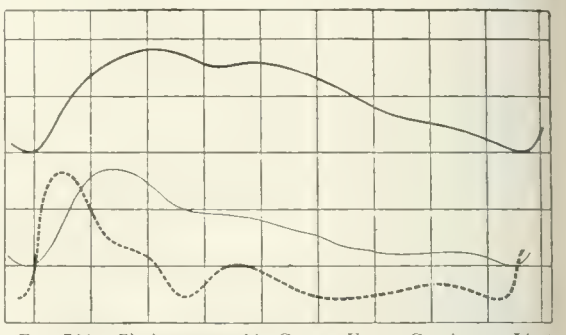

Fig. 722.—Plethysmographic Curve (Upper Continuous Line) Pulse Curve (Lower Continuous Line), and the Velocity Curve (Interrupted Line) in Man. (According to Fick.) To be read from left to right.

general anesthesia or after prolonged confinement to bed by accident or disease. In such cases an erect posture becomes dangerous owing to the gravitation of the blood to the abdominal organs and lower extremities with the result of lowering general arterial pressure. A recumbent position under such conditions favors the maintenance of the normal circulation. While the hydrostatic effect does not aid the circulation of the blood, it does affect considerably the pressure in the vessels. This effect on pressure must be taken into account in all blood-pressure determinations in clinical observations upon man and for purposes of comparison these should always be standardized by reducing them to the so-called heart-level. Certain observations on the pressure in the veins and capillaries of the foot should be mentioned in this connection. The result showed that the pressure in these vessels was but little higher than in the veins and capillaries of the hand. The effect of gravity is evidently neutralized by the compensating mechanisms and the return of the blood from the veins of the lower extremities must be ascribed largely to the effect of muscular contractions which by virtue of the valves of the veins force their contents upward past Poupart's ligament into the abdomen. This accounts for the familiar discomfort from standing still for any length of time and emphasizes the importance of exercise for the maintenance of a good venous circulation.

5. *The Time of a Complete Circulation.*—This was first determined by Hering (1829) by injecting potassium ferrocyanide into the central end of the jugular vein and observing the time of its first appearance in the bood issuing from the peripheral end of the same vessel. To reach the latter point a complete circuit had to be made, and the time thus determined was found to be 31.5 seconds in the horse, 16.7 seconds in the dog, 7.79 seconds in the rabbit. The time is not much affected by the length of the course in the same animal, because the difference between the longest and shortest path would be made up mostly of the larger trunks, where the rate of flow is most rapid. Dividing the time in seconds given above by the length of the cardiac cycle for the corresponding animal, it appears that the circulation time covers from twenty-six to twenty-eight heart beats. This

same rule applied to man would give as the circulation time:

$$27 \times \frac{60}{72} = 22.5 \text{ seconds.}$$

These measurements possess only a relative value, because the method does not take into account the errors arising from the diffusion of the salt during the time of its transit and from the fact that the first appearance of the salt is really determined by the maximal or axial velocity of the current. The mean time should therefore be taken as at least twice as great as the observed time. A simple method based on measurements of the electrical conductivity of the blood was introduced by Stewart for the determination of the circulation time of individual organs. His results on a large dog, weighing about twelve or thirteen kilograms, were as follows: Pulmonary circulation, 9 seconds; renal, 13 seconds; spleen, 11 seconds; stomach and intestines, about 9 or 10 seconds. He estimated the time of the lesser circulation in man at 12 to 15 seconds and of a complete circulation at approximately 60 to 75 seconds. As the entire blood passes through either ventricle in the time of a complete circulation the output of the heart at each systole, the so-called "pulse-volume" of the heart, may be deduced from these estimates. According to Hering's figures it amounts to approximately 100 c.c. of blood, while Stewart's result places it nearer to 50 c.c.

6. *The Pulse.*—The pulsatile character of the circulation in the arteries has been referred to in more than

Fig. 723.—Sphygmogram taken from the Radial Artery with a Marey Sphygmograph. (According to Langendorff.) Read from left to right.

one connection. With each systole of the ventricle a temporary increase of pressure and velocity above the mean results from the sudden accession of the extra volume of blood to that already present in this part of the system. The pressure oscillations are readily felt in superficial arteries, and the resulting expansion has long been known technically as the "pulse." It can be graphically recorded as Vierordt first showed (1855) and Marey soon afterward (1860) devised his well-known sphygmograph in order to obtain an accurate reproduction of the movement in all its phases. When recorded on a traveling surface, the curve or sphygmogram like that represented in Fig. 723 is obtained. The rise of the curve is quite sudden, while the downstroke is more gradual and interrupted by one or more secondary waves. The phenomenon of the pulse is entirely explained by the interaction of a number of physical factors, resulting as it does from the sudden injection of the contents of the ventricle into the elastic arteries, which are already full and whose outlet is partially blocked by the peripheral resistance. The actual height and form of a given pulse-curve depend much on the adjustment of the instrument; but if a series of curves are taken from different arteries under the same conditions, it is found that their character undergoes definite changes according to the distance of the corresponding arteries from the heart. The carotid curve, for example, rises higher and more suddenly than the radial curve; this in turn is higher and steeper than the tibial pulse curve. That is to say, the distention of the arteries diminishes both in rapidity and extent toward the capillaries. The rapid development and great amplitude of the pulse near the heart is the immediate result of the suddenness with which the ventricle is emptied. The additional quantity of blood thus thrown into the arteries starts a wave of positive pressure down the arterial tree, but on account of the resistance ahead it first expands the aorta and its largest branches. The distant arteries, therefore, do not feel the direct force of the systole, as would be the case in a system of rigid tubes; when the wave reaches them it has been damped by a longer or shorter stretch of elastic arterial wall. The recoil of this wall is less sudden than the contraction of the heart, and so the expansion of the successive segments becomes more gradual. The loss in amplitude is also readily explained by the elasticity of the arteries and the increase in the width of the stream bed. As the wave of positive pressure spreads over the arterial tree each section in turn expands to store a portion of the blood thrown out by the ventricle. By the time the smallest arteries are reached, the addition to their contents is both absolutely and relatively smaller. Under certain circumstances the pulse may pass through the capillaries into the veins beyond. The increased vascularity of organs during periods of heightened functional activity is secured by wide dilatation of their small arteries. The peripheral resistance, so essential in bringing the elasticity of the arteries into play, is thereby locally diminished and the dilated vessels cease to do their share toward destroying the remnant of the pulse which comes down to them from the larger arteries. The blood flows more readily through the widened channels, and may issue from the corresponding veins in a rapid pulsating stream. This systolic venous pulse appearing under special conditions in the small peripheral veins, must be distinguished from the pulsations observed in the large veins near the heart. The latter are produced by pressure variations developed in the auricles and transmitted backward along the great veins, and have recently attracted considerable attention on the part of clinicians. This so-called venous pulse gives a tracing which is somewhat varied and complicated, but usually shows three positive waves commonly designated as the *a*, *c*, and *v* waves (Fig. 724).

The *a* wave is presystolic in time and is caused by auricular systole; it is separated by a brief negative wave from *c*, the first systolic wave, which occurs in the beginning of the ventricular system and is ascribed to the sudden closure and protrusion of the tricuspid valve. During the period of discharge, when the base of the ventricle descends toward the apex, the pressure falls again, to be followed by the second systolic or *v* wave due to the gradual filling of the

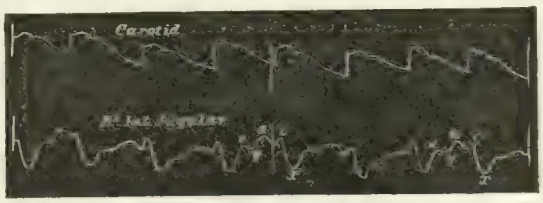

Fig. 724.—Simultaneous Tracings of the Carotid Pulse and of the Jugular Pulse; showing exact synchronism of the carotid pulse with the carotid wave (*c*) of the jugular pulse. (Mackenzie, The Study of the Pulse, 1902.)

auricle and eventually to the return of the base of the ventricle to its diastolic position. This wave may show secondary undulations. Finally there appears a third negative wave as the tricuspid valve opens and the blood rushes from the auricle into the ventricle, the so-called postsystolic vacuum of Chauveau and Marey. Simultaneous records of the pulse in the arteries and veins throw light on the pressure changes in the heart, on the condition of the heart valves, and on the rhythm of auricles and ventricles and therefore

possess great clinical value. For details regarding the special features of pulse curves, including the number and character of the secondary elevations in the arterial sphygmogram and the variations observed in health and disease, in both arterial and venous tracings the reader is referred to the special article on the pulse (see *Cardiography* and *Sphygmography*).

The rate of transmission of the pulse wave, which must not be confounded with the onward movement of the blood itself, is found by taking simultaneous records of the pulse from arteries unequally distant from the heart. If the distance of the two points from the heart is known, the rate of propagation is easily calculated, and it has been found to vary normally between five and ten meters per second. The rate depends mainly on the degree of rigidity of the arteries, the wave traveling slowly when the mean blood pressure is low and in the soft distensible arteries of children, while its velocity is increased by high arterial pressure and the hardening of the arteries in old age. In any case the pulse wave moves many times faster than the blood itself, being, as we have seen, merely a wave of pressure which is started in the aorta and which travels over the blood exactly as a water wave passes over the surface of a stream independently of the rate and direction of the latter's own current. The ordinary pulse curve does not return to the base line from which it started until the rise due to the next wave begins, indicating that the wave requires the entire time of a cardiac cycle to pass a given point. With a heart beating at the rate of seventy-two per minute, this would equal $\frac{60}{72}$ second, and taking the velocity of the wave at six meters per second, we would have as the length of the wave $6 \times \frac{60}{72} = 5$ meters. This is several times greater than the distance of the farthest capillaries from the heart, showing that the beginning of the pulse wave is lost at the periphery some time before the end of it leaves the aorta.

7. *The Pulmonary Circulation and its Relation to the Systemic.*—The maintenance of the circulation as a whole implies that the average output of the two ventricles of the heart is the same. Considering the relatively small capacity of the pulmonary circuit, which normally contains only one-twelfth of the total blood (Hegel and Sprehl), possibly one-fifth according to Stewart's measurements of the pulmonary circulation time, the time spent in this part of the vascular system must be shorter than that taken for the major circuit (Stewart). The pressure in the pulmonary arteries has been measured upon various animals by numerous observers with very discordant results; in general it seems to range between one-eighth and one-fifth of the aortic pressure, being given at 20 to 25 mm. Hg. for the dog. This indicates a low resistance in the pulmonary capillaries, and the great distensibility and slight tone of the pulmonary vessels are perhaps the most striking features of the lesser circulation. The pressure in the pulmonary circuit shows less frequent and less extensive variations than those observed on the systemic side, and the changes which do occur seem to be determined mainly by mechanical factors. Among these the varying conditions in the systemic arteries and veins and the state of distention of the lungs may be mentioned. The influence of the respiratory movements on the pulmonary circulation is a complex one and depends on several factors. The expansion of the lungs in a normal inspiration has been shown to dilate the pulmonary vessels. This diminishes the resistance and tends to lower the pressure in the pulmonary artery. At the same time the output of the right ventricle is augmented by the increased aspiratory action of the thorax, which we have seen hastens the return of the blood to the right auricle and so increases its diastolic distention. This factor would tend to raise pulmonary pressure, and actual measurement alone can determine which of the opposing tendencies will have the upper hand. In certain cases, at least, it has been shown that the dilatation more than compensated for the increased output of the heart and the pressure in inspiration fell (Talma). In natural expiration the conditions are reversed and the pressure again rises. The course of events is entirely different during artificial respiration, when the lungs are inflated under positive pressure with the thorax open.

The great range of adaptability, as regards its capacity, shown by the pulmonary circuit deserves special mention. In dogs about three-fourths of this vascular area was occluded without producing any effect on aortic blood pressure (Lichtheim). Since the systemic venous pressure in this experiment also remained normal, the amount of blood passing through the lungs was evidently not reduced by this extensive narrowing of the path. The pressure in the remaining pulmonary artery was, however, raised by the operation, and it is supposed that this rise of pressure distended the open channels sufficiently to explain the undiminished flow through the lungs. It is doubtful whether this observation, made under abnormal conditions, can be applied generally; at least in rabbits with pleural cavities intact clamping of one pulmonary artery caused a decided drop in the systemic blood pressure. It is merely given to illustrate the possibilities of capacity changes in the lung vessels. They can easily be distended so as to retain enough blood to lower the carotid pressure to zero, as shown in experiments on differential respiration.

By their extensive adaptability the pulmonary vessels protect the right ventricle against excessive back pressure and at the same time regulate the diastolic filling and so the work of the left ventricle, somewhat as the "venous cistern" composed of the large thoracic and abdominal veins, regulates the work of the right ventricle. The pulmonary circulation is affected not only by the condition of the systemic circuit at its venous end, but also by that on the arterial side. An excessive transfusion or a powerful general constriction may so increase the work of the left ventricle that it fails to empty itself completely at each systole. A stagnation extending from the left ventricle to the left auricle and thence to the pulmonary veins results, and the pressure in the lesser circuit is raised. The threatened danger from this source to the right ventricle with its thin walls is averted by the power of expansion which has been dwelt upon so fully, so that the lungs may be said to play the same rôle in regulating the blood flow to the left ventricle as that ascribed to the liver for the right ventricle (Tigerstedt).

8. *Respiratory Changes of Blood Pressure in the Systemic Arteries.*—The pulmonary circulation reacts upon the systemic pressure by modifying the inflow to the left auricle. It has been stated that the pulmonary vessels are expanded during inspiration and constricted during expiration. While the distention is in the act of developing, the blood flow is momentarily retarded and the left heart receives a smaller charge; but once the maximal dilatation has been reached, the resulting diminution of the resistance will augment the flow and the left heart receives a more abundant supply. On the contrary, expiration primarily increases the flow by narrowing the caliber of the dilated vessels and forcing on their contents, and secondarily diminishes it by increasing the resistance. The effect of these changes in the lungs on the pressure in the aorta depends largely on the rate and depth of the respiratory movements. When these are very shallow, no effect whatever is observed in the systemic arteries. When they are both quick and strong, only the primary effects appear, and the aortic pressure falls in inspiration and rises in expiration. The typical result is seen only in ordinary breathing when the rate is slow enough to permit

both the primary and secondary changes to produce their proper effect (see Fig. 725). In this case the pressure first falls during inspiration to a minimum (primary effect) and then rises again (secondary effect); in the succeeding expiration the rise continues for a short time to the maximum (primary effect) and then the pressure falls again (secondary effect). The main effect of inspiration, therefore, is to raise the pressure and the main effect of expiration to lower it. The curve frequently shows also changes in the rate of the heart which beats slower during expiration and faster in inspiration. These heart-rate changes are brought about through nervous

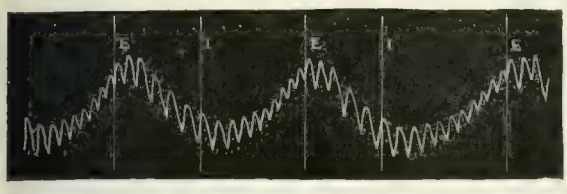

Fig. 725.—Carotid Blood-pressure Tracing of Dog. Vagi not divided. *I*, Inspiration; *E*, expiration. (Stirling.)

influences that must be considered later, and it need only be stated in this connection that they are not of sufficient moment to affect the general course of the phenomena here described.

The Mechanics of the Heart.—The circulation of the blood through the vessels is maintained by the energy of the beating heart. Before considering the causation and regulation of the beat, it will be convenient to take up a number of mechanical problems which the heart presents when regarded as a valvular pump in action.

1. *External Phenomena of the Beat.*—(*a*) When the living heart is observed directly either in a mammal or, better still, in a cold-blooded animal like the frog or terrapin, each beat is seen to begin with a contraction of the great veins in the neighborhood of the heart. The contraction proceeds as a peristaltic wave whose progress can be readily followed in the cold-blooded heart as it spreads over the auricles and then over the ventricles. In the mammal the wave-like character of the beat is difficult to recognize on account of the great rapidity of the movement. Here the auricles appear to contract suddenly over their whole extent, the auricular appendages being drawn inward and the rest of the wall pressing toward the auriculoventricular orifices, without, however, completely obliterating their cavities. As soon as the contraction of the auricles is completed the ventricles immediately follow with theirs. The contraction of each section of the heart is spoken of as its systole, and the succeeding relaxation as the diastole. A complete beat or "cardiac cycle" comprises an auricular and a ventricular systole and a heart pause, during which all parts of the heart are at rest. The systole and diastole of the two auricles are perfectly synchronous in a normal heart as are also those of the two ventricles, the synchronism resulting from the peculiar arrangements of the muscle fibers in their walls. In the auricles these consist of a superficial set common to both sides and of deeper fibers proper to each. The superficial fibers run transversely, being best developed on the anterior surface, and some of them turn in at the auricular septum. Of the deep fibers, some pass over the auricle in the form of an open loop to be attached at both extremities to the auriculoventricular ring; these are called "looped" fibers. Others, known as "annular" fibers, encircle the auricular appendages and surround the openings of the venæ cavæ and pulmonary veins. The complex nature of the arrangement of the fibers in the ventricles appears from the fact that a vertical section of their walls taken at almost any point shows the fibers on the outer surface crossing the direction of those on the inner, while between these every intermediate direction may be represented. The left ventricle possesses a much more powerful musculature than the right ventricle, but, as in the case of the auricles, a large number of fibers are common to both; in fact,

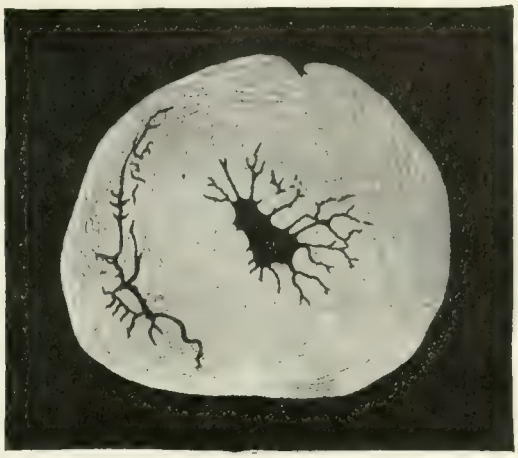

Fig. 726.—Cross-section of a Completely Contracted Human Heart, at the Level of the Lower and Middle Third. (According to Krehl.)

the outer wall of the right ventricle is so largely made up of fibers coming from the left that the former appears in sections of the heart like a cleft or pocket in the wall of the latter (see Fig. 726). Schematically, the fibers may be described as falling into a number of more or less well-defined groups according to the general direction of their course. The superficial oblique fibers constitute the first of these groups.

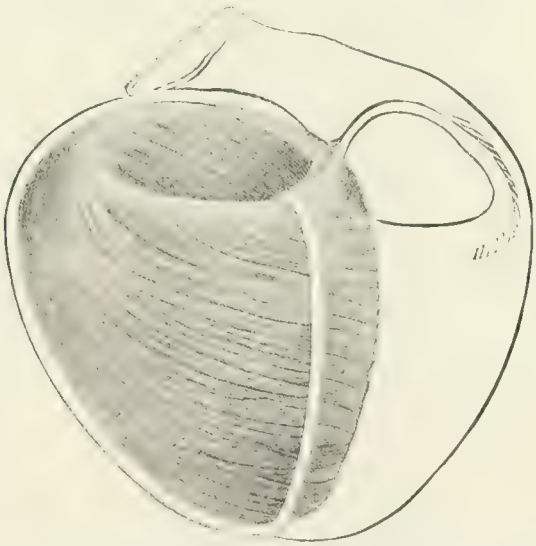

Fig. 727.—Intermediate Layer of Circular Fibers of the Left Ventricle. The outer and inner fibers have been removed, and the outlines of the entire heart schematically indicated. (According to Krehl.)

They take their origin in the fibrous rings at the base of heart and have a general trend obliquely downward and to the left. They form a thin, superficial stratum on the wall of the right ventricle, but on the left side they increase greatly in number, and on reaching the apex many of them turn in to form the

whorl, whence they ascend on the inner surface to terminate in the papillary muscles and chordæ tendineæ or to pass all the way up to the auriculoventricular ring. Mall divides these superficial fibers into two groups, the superficial bulbospiral and the superficial sinospiral fibers. Between the inner and outer layers thus formed, fibers with a more transverse or circular direction are met (Fig. 727). Some of these, the deep bulbospiral fibers, encircle the left ventricle and these are strongly developed. Others arising from the posterior side of the left ostium venosum pass transversely to enter the interior of the right ventricle and then turn upward toward the base. At the base of the heart some of the fibers of the bulbospiral system encircle the root of the aorta and the left ostium, while on the right side the sinospiral system forms circular loops round the conus arteriosus. A recent contribution of great importance in the physiology of the heart is the discovery that tendinous tissue does not completely separate the musculature of the auricles and ventricles of mammalian hearts. A band of modified cardiac muscle,

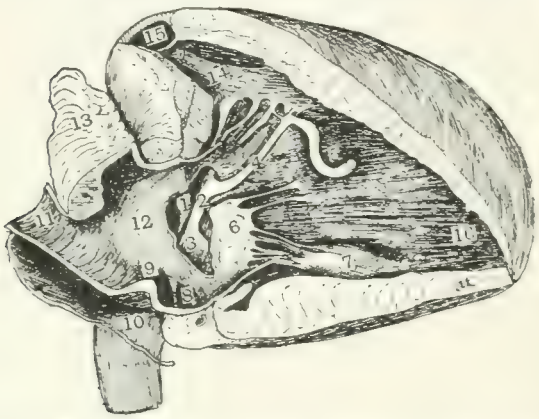

Fig. 728.—The Right Auricle and Ventricle of a Calf's Heart Exposed to Show the Course and Connections of the Auriculoventricular Bundle. (Keith and Flack, *The Lancet*, August 11, 1906.) 1, central cartilage exposed by dissection; 2, the main bundle; 3, auricular fibers from which the main bundle arises; 4, right septal division; 5, moderator band; 6, septal cusp of the tricuspid; the upper part of this cusp and the adjacent part of the infundibular cusp have been removed; 7, posterior group of the musculi papillares; 8, orifice of the coronary sinus; 9, so-called "tubercle of Lower" above the orifice of the inferior vena cava; 10, orifice of the superior vena cava; 12, septal wall of the right auricle; 13, appendix of the right auricle; 14, septal wall of the infundibulum; 15, beginning of the pulmonary artery; 16, apex of the right ventricle.

known as the auriculoventricular bundle, beginning near the posterior margin of the base of the interauricular septum, has been traced along the top of the interventricular septum until near the root of the aorta it divides into two main branches. One of these enters the right ventricle, the other the left, to pass down the septal wall, beneath the endocardium, until they break up into a system of strands over their inner surfaces. In the human heart the bundle is only about eighteen millimeters long and two millimeters wide, but it undoubtedly affords a muscular bridge by which the excitation wave is carried from the right auricle to the ventricles (Fig. 728).

The anatomical basis for the observed synchronism of the two sides of the heart is thus provided for in the large number of fibers which pass across and are common to the chambers of the same name. The progressive character of the contraction, not easily recognized by direct observation, can be demonstrated by means of the accompanying electrical phenomena which are similar in the case of the heart to those observed in skeletal muscle. An electrical change or current of action accompanies each heart beat; in the frog's heart the variation shown by the capillary electrometer is diphasic (Fig. 729). For the human heart the later work seems to show a triphasic current: first, base negative to apex, then apex negative to base, and then again base negative to apex. The accompanying curve has been constructed to represent these electrical variations (Fig. 730). From them it is inferred that the contraction begins at the base of the heart and advances toward the apex; that for a time (the interval *S* to *T* in the curve) the entire ventricle is uniformly contracted;

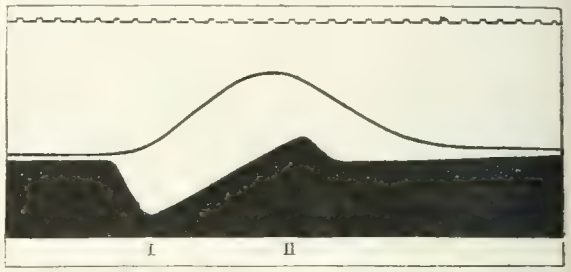

Fig. 729.—Simultaneous Photogram of a Single Beat (Black Line) and of the Accompanying Electrical Change, indicated by the level of the black area, which shows the varying level of mercury in a capillary electrometer. I, First phase, base negative to apex; II, second phase, apex negative to base. (Waller.)

finally, that the contraction ends by disappearing first at the apex. It evidently follows the recurrent path of the superficial oblique fibers beginning and ending at the auriculoventricular groove. Another deduction drawn from the electrical phenomena of the heart is that its contraction is comparable to a simple muscle twitch and is not to be regarded as a summated or tetanic contraction.

(*b*) Changes in the Form and Position of the Heart.—In diastole the heart can hardly be said to possess a definite shape of its own, although it is frequently described as a hemispheroid with a rounded apex and somewhat flattened anterior and posterior surfaces.

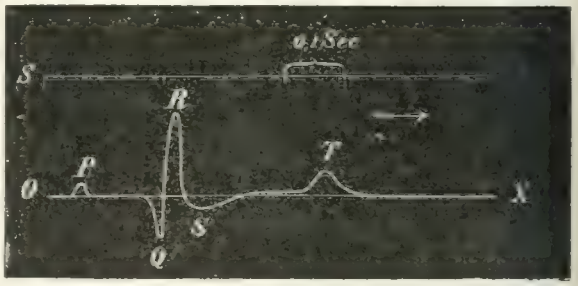

Fig. 730.—Diagrammatic Curve of the Action Currents of the Human Heart. (Einthoven.) *R*, Beginning of ventricular contraction; *S*, apex negative to base; *T*, third phase, base negative to apex. The small diphasic variations represented by *P* and Q are caused by the auricular systole.

On account of its soft, flabby condition its shape changes according to the position of the body under the influence of its own weight. Not so in systole; the heart then becomes hard and rigid and its shape approaches that of a regular cone with a circular base. The changes in the three diameters during this transition must depend on its previous form in diastole. Under normal conditions in which the heart is supported by the lungs as by an elastic cushion, there is probably no extensive flattening in any one plane. In this case entrance into systole would involve a shortening in all directions while the

apex became sharper or more pointed. When the heart is examined in the ordinary way in animals with open thorax, it unquestionably flattens out during diastole, the transverse diameter elongates at the expense of the anteroposterior, and the base takes the form of an ellipse. In this case when the elliptical base passes into the circular systolic form, the transverse and the longitudinal axes shorten, while the anteroposterior diameter increases in length. On account of the oblique spiral direction of many of the fibers, the apex is also seen to rotate somewhat to the left and forward, and the longitudinal axis approaches the vertical to the plane of the base. As regards the displacement of the heart as a whole, it is interesting to note that the apex is the stationary point, while the base is drawn toward it in proportion to the decrease in the longitudinal axis. The suspension of the heart from the large arteries should a priori make the base the relatively fixed point; its movement toward the apparently free apex is explained by the recoil of the blood as it is driven forcibly through the arterial ostia and by the elongation of the great vessels under the increased systolic pressure.

The effect of the contraction upon the cavities of the ventricles consists in their more or less extensive obliteration. Examination of maximally contracted hearts after death shows, however, that this is not complete. On the left side the short tubular chamber of the relaxed organ is reduced in systole to a mere stellate slit at the level of the papillary muscles, while above their summits this slit widens to an appreciable space of an irregular conical form (Fig. 726). In the right ventricle also, when the crescentic cavity is reduced to a mere slit by the approximation of the outer wall to the septum, an appreciable opening is left in the upper part below the tricuspid valves, and more especially in the region of the conus arteriosus. Recent measurements of the volume changes of the ventricles by means of Henderson's cardiometer would indicate a less complete emptying of their cavities than is generally assumed, and that the amount of blood remaining behind varies with the rate of beat and other conditions.

(*c*) The Apex Beat.—At each systole of the ventricles a shock or impulse may be felt in the fourth or fifth intercostal space about an inch below and a little

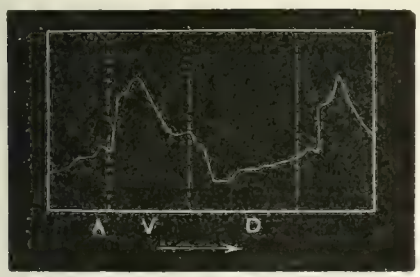

Fig. 731.—Cardiogram Taken with Marey's Cardiograph. *A*, Auricular systole; *V*, ventricular systole; *D*, diastole. The arrow shows the direction in which the tracing is to be read.

to the median side of the left nipple. This is where the apex lies against the chest wall uncovered by the lungs, and hence the name "apex beat" or "cardiac impulse" for this familar phenomenon. In diastole the flaccid wall of the heart yields to the more rigid thorax and the apex is not perceptible to the touch. The sudden hardening of the ventricles as they contract upon their contents enables them to exert pressure against the chest wall so that now the apex can be felt distinctly, its contact with the thorax being made even closer by the forward rotation already referred to. The elevation of the chest thereby produced can be recorded graphically and the tracings obtained are known as cardiograms (Fig. 731). The cardiogram gives valuable information as to the pressure and volume changes of the heart; its analysis will be attempted in connection with records of the heart's action taken by other methods. Special interest attaches to these curves from the fact that they represent the only direct record of the heart beat that can be obtained from man.

(*d*) The Heart Sounds.—Another physical sign by which the heart's action can be studied are the sounds which it emits. Normally, two sounds differing in pitch and duration, are audible in each cardiac cycle; the first a comparatively long, dull, booming sound, the second a short, sharp, sudden one. The interval between the first sound and the second is very short, but between the second and the succeeding first sound there is a distinct pause. The first sound is coincident with the systole of the ventricles, more particularly with the closure of the auriculoventricular valves, and it is generally regarded as a mixed or combination tone in regard to its origin. It can be heard distinctly in a contracting empty heart (Ludwig and Dogiel), so that it is partly at least a muscle tone. At the same time, it is probable that in the normally beating heart the sudden closure and tension of the auriculoventricular valves throw them and the blood into vibration, and it is possible that similar vibrations arise at the opening of the semilunar valves (Tigerstedt). The sounds resulting from these vibrations by fusing with the principle element, the muscle sound, have some share in the total effect and thus help in determining its final character. The second sound which marks the end of systole is purely valvular in origin, being produced by the closure of the semilunar valves. A sound exactly similar in quality can be obtained from the excised aorta by producing sudden tension of its valves. Considering the mode of production of the heart sounds, it is evident that each side of the heart must have a first and second sound of its own, making a total of four sounds. The fact that only two are ordinarily heard (the two first sounds fusing together and similarly the two second sounds) proves again the perfect synchronism of the two ventricles. A third heart sound may be heard in certain individuals according to a number of observers, and its existence has been demonstrated objectively by Einthoven by means of the microphone and string galvanometer. It occurs early in diastole, soon after the second sound and is heard most distinctly over the apex. It is most probably produced by the vibration of the auriculoventricular valves set up by the sudden inrush of blood from the auricles at the moment of the "postsystolic vacuum." Pathological alterations affecting the structure of the valves or of the cardiac muscle may dissociate the elements of the mixed sounds, modifying their usual character and quality and even giving rise to new ones. These abnormal sounds are known as cardiac murmurs, and from a study of their rhythm, their position of maximal intensity, and the direction in which they are propagated information of great diagnostic value is obtained.

Internal Events of the Beat.—(*a*) During diastole, when the whole heart is at rest and its chambers relaxed, the semilunar valves are closed by the high pressure in the arteries. The blood, returning in the veins with a fair velocity and under low pressure, meets with no resistance and enters freely into the auricles, and thence passes onward into the ventricles. The auriculoventricular valves at this time are open to the blood stream, but their cusps are more or less approximated by the eddies which return along the walls of the ventricles and carry the blood between them and the valve flaps. Presently the systole begins at the sinoauricular node and spreads quickly over the auricles. Without completely emptying themselves, they drive part of their contents into the

ventricles where the pressure is lower than in the veins, and thus complete the filling of those chambers. The same reflux currents which previously floated up the cusps continue for an instant after the flow into the ventricles has ceased, and thus the edges of the valves are brought into apposition even before the ventricular systole begins. Their perfect closure is facilitated by the anatomical arrangement of the papillary muscles and chordæ tendineæ (see Figs. 732 and 733). Each auriculoventricular valve may be regarded as a membranous tube attached to the auriculoventricular ring by one end along its whole circumference while the other end is deeply incised so as to form a number of separate flaps. These are attached to the inner surface of the ventricle and papillary muscles by tendinous chords arising not only from their free edges but also from their under surfaces. Each flap, moreover, sends its chordæ to more than one papillary muscle, and each of these in turn is attached to more than one valve flap. As the systole of the ventricles begins and the pressure on their contents increases there is no regurgitation into the auricles. The pressure secures more firmly the apposition of the thin free edges of the valves, and as the latter are put under sudden tension the first sound is heard. The chordæ tendineæ prevent the eversion or extensive bulging of the valves into the auricles, while the papillary muscles, contracting along with the rest of the heart muscles, serve to take in any slack in the chordæ which might result from the approximation of the base and apex, and so keep them taut. An accessory factor in the closure and support of the valves which deserves mention is found in the reduction in the size of the base of the heart during systole with its consequent narrowing of the auriculoventricular apertures. The pressure continues to rise in the ventricles until it exceeds that in the arteries, when the semilunar valves open and the discharge begins. The pressure on the arterial side of these valves being always considerable, their opening must not be thought of as a sudden bursting open with the separate folds thrown against the wall of the artery, but rather as a gentle yielding as the pressure on the ventricular side gains the upper hand. The free edges of the valvular folds are considerably removed from the walls of the sinuses of Valsalva, and this taken in connection with the thick projecting muscular cushions at the arterial apertures, reduces the opening through which the blood is discharged to a somewhat narrow slit. Eddies and whirls are formed in the wider space beyond, constantly tending to bring the valves together, and the moment the outflow from the ventricle ceases they close with such rapidity that no regurgitation occurs and the second sound is produced. The ventricle once more relaxes, the auriculoventricular valves open under pressure from the auricular side, producing the third sound, and the cardiac cycle is finished.

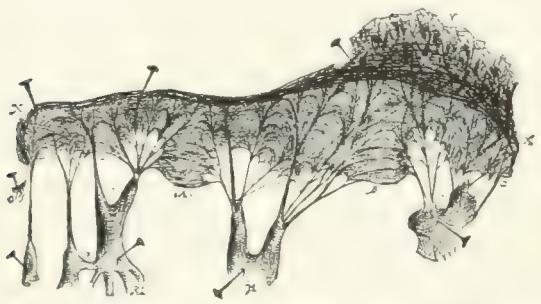

Fig. 732.—Human Tricuspid Valve—Ventricular Surface Spread Out Flat. *A*, inferior; *B*, anterior; *C*, septal segment; *D D′ D″*, lesser segments; *M*, anterior papillary muscle; *O O′*, papillary muscles attached directly to ventricular septum; *P*, papillary muscle attached to columnæ carneæ; *R R′ v*, portion of right ventricular wall, showing bundles of fibers continuous with chordæ tendineæ; X X′, line of insertion of segments into auriculoventricular ring.

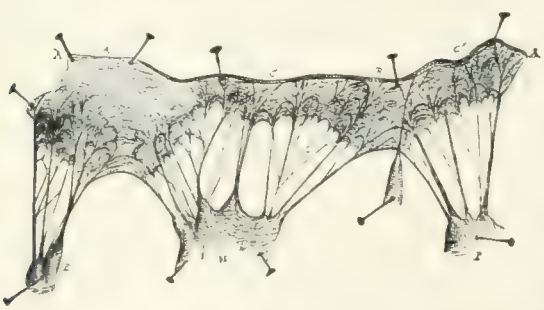

Fig. 733.—Human Mitral Valve—Ventricular Surface Spread Out Flat. *A*, Largest cusp close to aortic valve, aortic segment; *B*, next largest cusp, parietal segment; *C C′*, lesser cusps; *M*, anterior papillary muscle; *P P′*, posterior papillary muscles; *T T′* method of branching of chordæ tendineæ; *X X′*, line of insertion of cusps into auriculoventricular ring.

(*b*) Intracardiac Pressures.—A record of the pressure changes in the several heart cavities during the course of a complete cardiac cycle gives the truest account of the force- and suction-pump action of the organ, and valuable hints for the determination of the time relations of the successive events which go to make such a cycle. Several methods have been devised to obtain the record, and while the curves differ considerably in some respects, certain general conclusions have been obtained from them. In the first place, the upper and lower limits of the pressure reached in the course of an observation extending over a series of beats can be accurately measured by means of a mercury manometer with valves attached so as to convert it into a maximum or minimum manometer (Goltz and Gaule). This method shows that the maximum pressure in the ventricles is distinctly greater than the mean pressure in the corresponding arteries, that of the left ventricle being about five times as great as that of the right. In an actual experiment DeJaeger found the maximum pressure in the left ventricle of the dog 200 mm. Hg., and in another case Fick found it 160 mm. Hg. The pressure in the auricles is considerably lower, the maximum as measured on the right side being usually given at 20 mm. Hg. The minimum pressures in the cavities of the heart may fall below that of the atmosphere. Thus, in the left ventricle of the dog, it varied from −52 to −20 mm. Hg., in the right ventricle it was −17 mm. Hg. and in the right auricle −12 to −7 mm. Hg. Such values, however, are obtained only when the chest is closed, and the negative pressure of the thorax is partly responsible for these low pressures.

When the heart was exposed, and the pericardium opened the lowest pressure in the left ventricle was −7 to −25 mm. Hg., and in the right −1 to −2 mm. Hg., according to Goltz and Gaule. This observation has been confirmed and denied repeatedly, but the balance of evidence seems to favor the view that the diastolic expansion of the heart walls may in itself produce a certain amount of suction depending largely on the force and suddenness of the foregoing systole. Various suggestions have been made to account for it. Starling refers it to a dilatation of the base of the heart by the high pressure in the roots of the aorta and pulmonary artery. During systole the base of the heart, including the orifices of the great arteries, is constricted. The dilatation accompanying the relaxation increases the capacity of the ventricles and so creates a negative pressure. A more efficient cause is probably found in the peculiar conditions surrounding the coronary circulation. The filling of

the blood-vessels in the walls of the heart should open up its cavities much in the same way that a double-walled bag is distended by filling in the space between the two layers. Brücke's theory of the "Selbststeuerung des Herzens" was, in fact, based on this sort of mechanism. It assumed that the semilunar valves were thrown back during systole far enough to prevent the entrance of blood into the coronary arteries, whose distention at that time would oppose the systole; but when at the onset of diastole, the coronaries are opened and the blood enters under strong pressure from the aorta, the diastolic expansion would be materially assisted. This theory has since been shown to be a curious mixture of truth and error. Martin and Sedgwick demonstrated that the pulse in the coronaries was

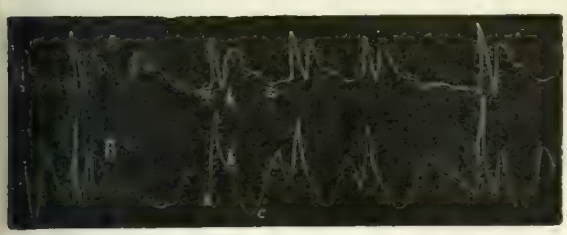

Fig. 734.—Showing Curves of Pressure (*A*) and Velocity (*B*) in the Coronary Artery of the Horse. (Chauveau and Rebatel)

synchronous with that in other systemic arteries; therefore Brücke was wrong so far as the mechanism by which the systolic dilatation of the coronary vessels is prevented is concerned. The semilunar valves do not close the orifices of these arteries. Measurements of the velocity of the blood flow in the coronary arteries by Chauveau and Rebatel have shown, on the other hand, that he was right as to the facts. Their curves (see Fig. 734) show that the tension and rate of flow both increase in the coronary artery at the beginning of systole (*a*); *i.e.* blood streams into it at this time. Then a second rise of pressure is observed during which, however, the velocity curve drops below the abscissa (*b*). This is the moment when the contraction of the ventricle becomes powerful enough to compress the intramural vessels and squeeze out their contents; hence the rise of pressure and the reversed current in the main vessel. Lastly, a new acceleration of the rate, not accompanied by a rise of pressure appears (*c*); the diastole has begun, the vessels are once more free, and the flow of blood through them is reestablished. Porter added new testimony on this point in the form of observations on the outflow from the coronary veins during different phases of the heart's action. Among other results he found that the volume of blood passing through the coronary vessels is increased by an increase in either the force or the frequency of the heart beat, the increase of volume being accomplished largely through the periodical emptying of the intramural vessels by the systolic squeeze of the fibers around them. Some other points of interest concerning the coronary circulation may be briefly mentioned in this connection. The branches of the main coronary arteries are functionally of a terminal character, as the anastomoses which exist are insufficient to provide collateral circulation. Therefore ligature of the individual branches results in infarction and necrosis of circumscribed areas corresponding to the distribution of those branches. The effect of such a ligature on the action of the heart as a whole seems to depend entirely on the extent of the area involved, arrest of the heart following ligature of the ramus circumflexus in 80 per cent. of the cases; of the R. descendens in 50 per cent., of the R. septi in 0 per cent., and of the A. coronaria dextra in 18 per cent. The ventricles in these cases of arrest went into fibrillar contraction (delirium cordis) a condition of incoordinated contraction, which may be induced also by injuries to certain parts of the heart and by strong electrical stimulation. As the ligation of the arteries supplying different areas produced fibrillation, the result is opposed to the idea of a definite coordinating center as proposed by Kronecker and Schmey on the basis of their needle-puncture experiments. Finally the relation between the volume of the coronary circulation and the rhythmical contractility of the heart muscle has been investigated by means of an artificial circulation, the applicability of which to the hearts of warm-blooded animals was demonstrated by Martin. The work shows that a surprisingly small flow suffices to maintain a rhythmical beat, the ordinary volume used in the experiments of McGrath and Kennedy upon vigorous cat hearts ranging from 3.5 to 13.5 c.c. per minute. Variations in the amount of blood fed to the heart influenced the force of the beats, while the rate was but little affected.

To return to the subject of intracardiac pressures, the oscillations between the limits given above must recur in the course of every cycle and the rate at which the pressure changes is very great. It has been estimated that the pressure within the left ventricle rises at the rate of more than 2,000 mm. Hg. per second. To obtain an exact record of such a change calls for an instrument with a quick response and low inertia; but the records obtained with the most improved spring manometers of recent years agree so nearly with the older curves of Chauveau and Marey in all essential points that we may assume for the present the correctness of their curves (Fig. 735).

The auricular curve shows a quick sudden rise of pressure which reaches its maximum in about 0.1 second, and returns again immediately so as to form a single rounded peak. The steep rise of the two lower curves (Fig. 735) shows that the ventricular systole follows immediately upon that of the auricles and that the pressure goes up with great rapidity. Then there follows a portion of the curves which goes

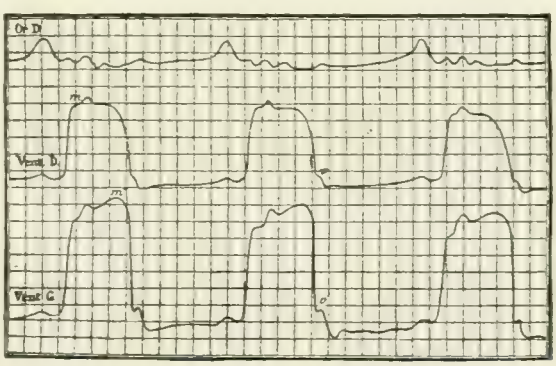

Fig. 735.—Endocardic Pressure Curves from the Horse. *Or. D*, Right auricle; *Vent. D*, right ventricle; *Vent. G*, left ventricle. (Chauveau and Marey.)

by the name of the "ventricular plateau" because it extends in a direction more or less parallel to the abscissa, sometimes rising, sometimes falling a little, according to the method used. It represents graphically the maintenance of contraction of the ventricles, their systole lasting about 0.4 second. The lever finally sinks back abruptly to the base line and beyond, as shown in the descending limb of the curve. Intraventricular pressure curves always present secondary elevations distributed over the main curve. They are not constant as to number or form, seemingly changing with the kind of instrument used, and some of them are unquestionably artefacts. Others corre-

spond to definite processes going on inside the heart, as, for example, the small wave which is nearly always seen preceding the large rise due to the ventricular systole. Its position shows that it is synchronous with the systole of the auricle, the effect of which on the pressure in the ventricle is thus recorded. There is no indication on the record either of the closure of the auriculoventricular valves or of the opening of the semilunar valves. An appreciable time must elapse after the beginning of the systole before the pressure mounts high enough to force open the semilunar valves against the arterial pressure; but this being a gradual process, as we have already stated, an effect in the form of a break or notch upon the curve would hardly be expected. By taking simultaneous records of the pressure in the left ventricle and in the aorta it has been shown that the pressure in the latter begins to rise about 0.1 second later than in the ventricle. The point on the curve which corresponds to the time of opening of the valves must be situated, therefore, near the top of the ascending limb and is not marked in any way. The same indirect method must be relied on to determine, upon the curve, the position corresponding to the closure of the semilunar valves. They will close, of course, the instant the pressure within the ventricle falls below that in the artery, and upon the curve must be represented high up on the descending limb not far from the beginning of the steep descent from the plateau. The curve again shows no record of this event. The duration of the component elements of a complete cardiac cycle is found most accurately from such records as have just been described. For the human heart, however, it must be estimated from observations on the heart sounds and from cardiographic and sphygmographic curves. Leaving out of account the slight differences in the figures as given by various observers, the duration of the phases of the human heart, beating at the rate of 70 per minute, may be stated as follows:

Ventricular systole	0.379 second
Ventricular diastole	0.483 second
	0.862 second
Auricular systole	0.1 second
Auricular diastole	0.762 second
	0.862 second

The heart pause in this case equals 0.383 second. The power of rapid recuperation of the musculature of the heart is impressively shown by these figures. Another point of fundamental importance should be noted in this connection. It will be shown later that the rate of the heart varies within wide limits at different times and under different conditions; but throughout these extensive variations the duration of the ventricular systole remains remarkably uniform. In man, for example, it has been found that the ventricular systole varied only between 0.382 second and 0.190 second when the pulse rate ranged from 32 to 124 per minute. The variations in the rate of the heart are essentially dependent on changes in the duration of the pause, while the systole is but slightly affected. Even the pressure in the arteries has been shown to have no appreciable influence on the duration of the systole, the heart apparently possessing in a high degree the power of adapting its work to the varying demands made upon it without loss of time.

(*c*) The Work Done by the Heart.—In considering the work of the heart it is treated practically as a force pump which discharges a certain volume of liquid with a known velocity against a given resistance. The auricles from this standpoint become unessential attachments to the apparatus, although physiologically they may be important enough. They not only provide reservoirs for the reception of the blood during the relatively long ventricular systole, thereby avoiding stagnation or damming back in the veins, but as we shall see later, they constitute a regulating mechanism for the work of the ventricles by determining both the rate of their beat and the extent of their charge.

The suction of the ventricles already explained is here also disregarded. This suction, together with that of the thorax as a whole, is favorable to the circulation in that it assists the return of the blood in the veins. It may be neglected at present as it is quite insignificant in comparison with the other factor concerned, and the blood would return to the heart without its aid under the influence of the impulse given to it by the heart at the arterial end.

The work done by the heart is expended in two ways: (1) The contents of the ventricles must be discharged against a resistance measured by the mean pressure in the aorta and pulmonary arteries. Taking the left side alone for the present, work will be done at each beat equal to $P \times R$, P being the "pulse volume" or the amount discharged in a single systole and R the mean blood pressure in the aorta. (2) Work is done in conferring upon the blood discharged a certain velocity. Now the kinetic energy represented by a mass in motion is expressed by the formula $\frac{1}{2}mv^2$, which if m equals the weight of a body under the influence of gravity, may be written $\frac{pv^2}{2g}$. Applied to the heart, p in this formula represents again the pulse volume, v the velocity in the aorta, and g the accelerating force of gravity, *i.e.* 9.8 meters (thirty-two feet). The total work of the left ventricle, therefore, equals $PR+\frac{Pv^2}{2g}$ and can be calculated when we know the pulse volume of the heart, the mean aortic pressure, and the rate of flow in the aorta. The two latter have been determined with a fair degree of approximation and may be taken at 150 mm. Hg. for the pressure and 500 millimeters per second for the velocity. Neither of these figures is perfectly exact, but the error introduced by inaccuracies in them has little effect on the result as compared with that due to our ignorance of the pulse volume. An exact determination of the latter would furnish the key to many problems in the mechanics of the circulation, and frequent attempts have been made to get at it. The estimates given for the human heart vary all the way from 45 to 188 grams; for the present 100 grams may be taken as a fair average, although the true result will probably be found somewhat less than this. Substituting the given values in the formula and making the correction for the specific gravity of mercury (13.6), we obtain as the work of the left ventricle:

$$w=(100\times0.150\times13.6)+\frac{100\times(0.5)^2}{2\times9.8}$$

or $w=204+1.28$ gram-meters.

The calculation for the right ventricle is made in the same way, the pulse volume of the two sides of the heart being assumed to be equal and the mean pressure in the pulmonary arteries being taken at two-fifth that in the aorta. The work of the right ventricle is therefore equal practically to two-fifths of 205.28, or 82.11 gram-meters. Multiplying the work of both sides (287.39 gram-meters) by the number of beats per minute (70) and by the number of minutes in twenty-four hours (1,440), the work of the heart done in one day is found equal to 28,969 kilogram-meters as a conservative estimate. This represents a considerable percentage of the total energy production in the body, when it is remembered that the mechanical work done by a man in eight hours is estimated at about 125,000 kilogram-meters and that the work of the muscles of repiration in twenty-four hours amounts only to 11,700 kilogram-meters.

(*d*) The Rate of the Heart.—It is a matter of some

practical importance to the physician to know the normal rate of beat of the heart, and on this account numerous statistics have been compiled with a view of determining the relative influence of the various conditions which affect it. Ordinarily the pulse rate presents more or less regular and extensive variations in the course of a day which are sometimes designated "diurnal." They are hardly the expression of an inherent rhythmicity, since they almost disappear when the subject rests quietly in bed and abstains from food and drink, but rather the result of the complex and ever-changing activities which make up the daily routine.

Among the physiological factors which affect the heart rate in any given individual are temperature and exercise. Experiments upon the isolated mammalian heart have shown that the rate varies directly with the temperature up to about 41° C. Beyond this optimum point, a further rise of temperature becomes harmful and quickly the lethal point is reached (45° C.). In fevers the acceleration of the heart usually amounts to eight or ten beats for every degree of rise in temperature. In typhoid, however, the change is less, in scarlet fever greater, indicating the implication of other factors. These temperature effects are direct on the cardiac muscle and may be contrasted with the indirect reflex changes produced by external temperature variations which act through the sensory nerves of the skin. The familiar effect upon the pulse rate of muscular exercise is both sudden and marked, and it may almost be stated as a law that the increase in the rate is proportional to the duration and intensity of the work done. On this account the pulse is slow during sleep, when the minimum is usually reached, and the increase in rate on sitting up or standing over that of the recumbent position is probably the result of the muscular effort involved in maintaining these upright positions. The effect of exercise may be quite transient or it may persist for a considerable time depending upon the duration of the work done. Thus a walk of a mile or two at a moderate gait will keep the pulse rate quickened for thirty or even sixty minutes thereafter, and this long-lasting after-effect must be taken into account whenever observations on the normal rate are to be made. Extensive data in which accidental variations from the preceding causes were guarded against have been tabulated in order to determine the influence of sex, age, and size upon the rate of the heart. The conclusion so far reached may be briefly summarized as follows:

Age.—The average pulse rate is highest the first year after birth, being given as 134 per minute in one series of observations; it sinks steadily up to the twenty-first year when a rate of seventy-two is reached; it remains at this level to about the sixty-fifth year, after which it begins to go up again slightly, rising perhaps to seventy-nine or eighty per minute at the eightieth year.

Size.—The differences just noted depend in large measure on differences in size, although age in itself apart from size has some influence. Taking the average of a great number of cases there is no doubt that tall individuals have a slower heart than smaller ones of the same age, the difference being as much as twenty-three beats per minute in the first year but sinking into insignificance later on in life.

Sex.—Comparing males and females of the same age, the pulse rate is found to be more rapid in the latter at all ages from the second year on. Women on the average are a little smaller than men, so that a correction for size should be introduced. Even when this has been done the general statement remains true, although the differences then are smaller than they ordinarily appear. The following tables, abridged from those given by Volkmann, furnish the basis of the foregoing generalizations:

TABLE I.

Age.	Heart rate.			Number of observations.
	Maximum.	Minimum	Average.	
0– 1	160	101	134	59
5– 6	128	70	98	56
10–11	106	56	87	73
15–16	112	66	83	77
20–21	99	59	71	67
30–35	104	58	70	125
40–45	104	50	72	105
50–55	94	52	72	42
60–65	100	54	73	60
70–75	104	54	75	44
80 +	98	63	79	31

TABLE II.*

Age.	Mean pulse rate.	
	Male.	Female.
2– 7	97	98
8–14	84	94
14–21	76	82
21–28	73	86
28–35	70	78
35–42	68	78
42–49	70	77
49–56	67	76

* The average rates in this table were obtained by Guy from twenty-five observations, in each case taken at midday upon fasting individuals who were at rest in a sitting position.

TABLE III.

Height in millimeters.	Mean pulse rate.	
	Male	Female.
525	158	144
875	110	107
975	101	106
1,075	97	98
1,175	91	94
1,275	88	95
1,375	87	87
1,475	85	84
1,575	75	77

From a teleological point of view the correlation between the pulse rate and the conditions enumerated above is easily understood. It provides an arrangement for adapting the circulation to the intensity of general metabolism through the rate of the heart. The smaller the size of the body, the greater will be the ratio of the surface to the mass and hence the more rapid the heat dissipation; hence to keep up body temperature heat production must be raised in the same proportion, *i.e.* greater metabolic activity is required which in turn demands a more active circulation and a faster heart. In the same way the chemical activity of the muscles is heightened by exercise and again the circulation is accelerated. The exact mechanism by which the quickened pulse is obtained is difficult to determine, being in most cases of a complex character. The effect is sometimes a direct one on the heart itself effected through the altered physical and chemical conditions of the blood; at other times it is mainly produced indirectly through the nervous

system by way of the extrinsic nerves of the heart; usually it is the combined result of various interacting factors.

The Regulation and Adaptation of the Vascular Mechanism.

A rigid circulatory system working with the regularity of a dead model and supplying each organ with the same steady stream of blood, irrespective of its needs, would by its very regularity work its own destruction. In a living organism there must be a continual adjustment in the blood supply to each part with every change in external or internal conditions. The regulating mechanism, as we actually find it, comprises two parts; one connected with the heart, which being central produces general effects only; the other with the peripheral blood-vessels, through which both local and general effects can be brought about. As usual, the coordination and regulation of the blood vascular system are obtained through the mediation of the nervous system, the relation of which to the heart and blood-vessels must now be described.

The Innervation of the Heart.—It is customary to speak of the nerve supply of the heart as consisting of an extrinsic and an intrinsic mechanism. The extrinsic nerves include efferent fibers, which are supplied by the vagi and the cardiac rami of the sympathetic chain, and which approach the heart at its venous end; and afferent fibers, which pass from the heart at its arterial end and are characterized by their larger size and the presence of the medullary sheath. In the mammal the extrinsic nerves terminate in plexuses around the arch of the aorta, and from these the intrinsic nerve supply is derived. Branches proceed to the junction of the great veins with the heart to be distributed to the various parts of the organ. Ganglia are abundant on the superior vena cava and are found also on the pulmonary veins, in the walls of the auricles, in the auriculoventricular groove, and for an undetermined distance down the ventricular walls. Both nerves and ganglia lie for the most part superficially under the pericardium, and as they are traced along the heart from the point of entrance it may be said in general that the proportion of medullated to non-medullated fibers goes on decreasing, and that the number of ganglion cells likewise diminishes, disappearing entirely at or near the apex. The ganglia are often classified as sinus ganglia and auriculoventricular ganglia. This separation into groups is obscure in mammals, but in the frog's heart comes out distinctly, the sinus ganglion located at the junction of sinus venosus and auricles being known as the ganglion of Remak, the auriculoventricular ones as the ganglia of Bidder. In the frog the vagus and sympathetic fibers reach the heart in a common trunk, one on each side, passing along the superior cavæ to the ganglion of Remak. From this, in addition to scattered fibers, two main cords, the anterior and posterior septal nerves, proceed to the ganglia of Bidder. From the latter small twigs penetrate the substance of the ventricle, scattered nerve cells occurring for some little distance along their path; but the lower part of the ventricle, perhaps the lower two-thirds, is said to be quite free from them.

1. *The Development of the Normal Beat.*—In order to appreciate the part played by the nervous apparatus of the heart, it will be necessary to consider the mode of development of its normal beat, of which the automaticity, the rhythmicity, and the regular sequence of the several chambers constitute the most striking features.

(*a*) Automaticity.—It has long been known that the heart of a cold-blooded animal will continue to beat for hours and even days after it has been removed from the body. There was every reason to think that the mechanism by which the beat is developed is the same in all the vertebrates, and much of the physiology of the heart as worked out on the frog was applied to the mammal. More recently H. Newall Martin succeeded in keeping alive the isolated heart of the latter also by supplying it with a suitable artificial circulation, and the question of its automaticity was definitely settled. The nerves reaching the heart from without were evidently not essential to the beat, for which all the conditions were contained within the organ itself. The heart is an automatic organ whose activity depends on some internal stimulus, and the question as to the nature of this stimulus and its point of attack immediately arises. Two answers have been given and are still current in physiology under the names of the "neurogenic" and "myogenic" theories of the genesis of the heart-beat. The neurogenic theory assumes that the excitation arises within the nerve cells at the venous end of the heart which act as an automatic motor center. Through a definite anatomical mechanism the impulses are distributed over nerve fibers and lower lying subordinate ganglia, thus accounting for the spontaneous origin of the beat, its orderly sequence and its coordination. The neurogenic theory is based on the following considerations: Muscular tissue in general, and especially the more highly differentiated types of it, depends upon its motor-nerve impulses to set it into action, whereas nerve cells constitute the automatic tissue of the body par excellence. Assuming similarity of function or properties in all nerve cells, those within the heart included, an easy explanation of the automatic beat of this organ would be furnished by the rhythmical motor impulses sent to the cardiac muscle by its intrinsic ganglion cells. Those who adopt this view urge in its support the interesting correlation between the number of ganglion cells distributed to each segment of the heart and the degree of spontaneity and rhythmicity which that part possesses. Thus upon the frog's heart, in which the normal beat begins in the large veins leading to the heart and sweeps over the sinus venosus, auricles, ventricle, and bulbus arteriosus in regular sequence, the following observations can be easily verified. When the heart in dying ceases to beat the several segments come to rest in turn, beginning at the arterial end. The ventricle fails first, then the auricles fail, and lastly the sinus venosus fails. Further, on testing the irritability of the quiescent heart from time to time by means of gentle mechanical stimulation, its eventual disappearance is found to follow the same order as the failure of the natural beat. Lastly, if by means of a series of transverse sections, carried through the heart at different levels, the ventricular apex alone, or the entire ventricle or the ventricle with some auricular tissue, be in turn separated from the venous end of the heart, it will be found that the sinus venosus possesses the greatest potentiality to beat, that the power of generating rhythmical spontaneous beats diminishes in the isolated piece as the plane of section approaches the apex, and that the apex itself will not beat spontaneously at all. The several segments of the frog's heart form, as regards their irritability and spontaneity, a descending series —sinus venosus, auricles, entire ventricle, lower third of ventricle—very similar to the series they form when arranged with reference to the number of contained nerve cells. The inference that the rhythmical beat is the result of the activity of these nerve cells is natural and though based upon observations upon the frog's heart, it has been extended to the vertebrates generally. Experiments on the heart of the horseshoe crab have shown that in this animal the beat depends on the integrity of its intrinsic nerve cells. As the muscular tissue of this heart differs in its fundamental properties from that of the vertebrate heart, the result cannot be applied to the latter. While the neurogenic theory in its latest form satisfies the logical requirements in explaining most of the known facts regarding the beat of the heart, no positive proof for

it can be given, and physiologists very generally have favored the alternative view.

The myogenic theory denies the immediate physiological connection between the ganglion cells and the development of the beat, and at present finds in them merely nutritive and distributing centers for the intrinsic nerve fibers, putting them on a level with the cells of the sympathetic ganglia rather than with those of the central nervous system. The origin and nature of the beat are referred entirely to the peculiar properties of cardiac muscle, and much evidence has accumulated in support of this view. It is known in the first place that hearts or strips of heart muscle entirely free from nerve cells may, under proper conditions, pulsate rhythmically in a normal manner. Not to speak of the invertebrate heart, it is a familiar fact that the heart begins to beat in the fetus long before any nerve cells appear in its vicinity, while a common laboratory experiment consists of suspending under slight tension a strip of the terrapin's ventricle and recording for hours its rhythmical contractions. In the second place cardiac muscle does possess peculiar properties not found in other forms of muscular tissue, properties which seem to afford an adequate explanation of the rhythmicity of the heart, while its automaticity and normal sequence are at least as easily explained on the myogenic as on the neurogenic theory. As to the causation of the beat on the myogenic theory, the suggestion has been made that the internal stimulus consists merely in the spontaneous dissociation of the contractile substance. Heart muscle is admitted to be less highly differentiated, histologically, than skeletal muscle, and may plausibly be assumed to have preserved in a greater degree the primitive and fundamental attributes of undifferentiated protoplasm. Its spontaneity would be an exhibition of the same property which is inherent in the ameba as well as in the ganglion cell and calls for no special explanation. The inner stimulus has also been sought in the products of its own metabolism, but no satisfactory evidence in support of this view has been obtained. The prevailing tendency of recent years has been to regard the blood or lymph as the most probable source of this stimulus. This idea arose in connection with the work on the nutrition of heart muscle. It was long assumed that serum albumin is a necessary constituent of artificial nutritive media for the isolated heart, the protein being added to the mixture directly or else supplied accidently by the residue of blood and lymph adhering to the meshes of the heart wall. For this reason, it was maintained, isolated hearts could be kept beating on a physiological saline solution for a comparatively short time only. It was found, however, that a heart which had been completely run down on 0.6 per cent. NaCl solution would beat again for a time if a small amount of Na_2CO_3 was added, and when it had come to rest on this mixture, could be revived a second time by the addition of soluble calcium salts, giving a long series of strong and regular contractions. These remarkable observations were the beginning of a prolonged study of the action of the inorganic salts upon the heart, which is still in progress. One result of this work has been to direct attention to the high degree of tonicity possessed by heart muscle. In normal diastole the heart does not relax completely; its stops in a condition of permanent partial contraction, which constitutes its tone. This is obvious on comparing the normal diastole of a heart with the extreme relaxation of complete vagus inhibition or of death. The tone or tonicity of the heart, measured by the extent of its diastolic relaxation, was found to vary with the reaction of the medium and with the kind and amount of inorganic salts present. Weak acids diminish, alkalies increase the tone, and a similar antagonism holds good between potassium and calcium salts. The tone of the heart is, therefore, intimately dependent on the nutritive exchanges going on within its substance, and its diminution or loss may be an important factor in cases of dilatation of the heart. The subject of tonicity of the heart thus becomes a matter of practical importance from the standpoint of clinical medicine. Another result was the discovery of the special relation of the inorganic salts, particularly of potassium and calcium salts, to the causation of the heart beat. Calcium not only diminishes relaxation and increases the tone, but it promotes contraction so that excess of this element brings the heart to a standstill in powerful systole (calcium rigor). Potassium produces the opposite effect, promoting relaxation and, when present in excess, causing the heart to come to rest in extreme relaxation (potassium inhibition). A normal rhythmical beat can be maintained only by preserving a proper ratio within comparatively narrow limits of these two classes of salts. From these and similar observations the conclusion has been reached that the beat of the heart normally is the result of the interaction of the inorganic constituents of the blood with the heart muscle, the former providing the adequate stimulus, the latter the irritable agent whose complex living molecule responds to the stimulus with an explosive decomposition and furnishes the energy of the contraction.

(*b*) Rhythmicity.—On the assumption made in the foregoing paragraph the stimulus to the heart is constant while the response is intermittent and rhythmical. This kind of relation between a continuous stimulus and an intermittent reaction is not peculiar to the heart, although it is perhaps most conveniently demonstrated upon strips of ventricular muscle. When these are suspended under a certain tension, the mechanical stretching of the fibers acting as a constant stimulus causes them to give a series of rhythmical contractions. The reason for this is found in the peculiar alterations in irritability which accompany the beat of the heart. When the contraction of the whole heart or of an isolated strip of heart muscle is recorded by means of a lever, the curve of contraction, after a relatively long latent period rises slowly to a maximum and as slowly declines again. The entire duration of it varies in different animals; but the curve shows an unmistakable resemblance to the simple contraction curve of skeletal muscle. The electrical changes in the heart accompanying its beat corroborate the view that the beat corresponds to a single twitch, and the dictum that "the heart knows no tetanus" has long been current in physiology. Recently Walther showed that under certain abnormal conditions a limited amount of fusion and summation of contractions, and hence incomplete tetanus, could be obtained in the case of the frog's heart; but normally this is not known to occur. The reason why heart muscle never gives tetanic contractions but responds rhythmically to rapidly repeated or constant stimuli is found in the so-called "refractory period" (Kronecker, 1874; Marey, 1876), which prevents fusion of contractions, and in the "law of maximal contraction" (Bowditch, 1871) which prevents summation.

When one stimulates a skeletal muscle with a strong stimulus, a large contraction follows; when a weak stimulus is applied, the contraction is small; within limits the contraction is proportional to the stimulus. Not so with the heart. The beat is always the best which the ventricle can accomplish at the time being, be the stimulus weak or strong, provided only it is efficient to provoke a response at all. With the heart it is "all or nothing." Moreover, the effect of a stimulus applied to the ventricle, when it is beating rhythmically either spontaneously or as the result of rhythmical stimulation, will depend upon the exact phase of the cycle of the beat at which it is thrown in. If it is thrown in just as a relaxation is taking place, a beat follows prematurely before the next beat would naturally follow, this premature beat being obviously

produced by the stimulus. But if it be thrown in while a contraction is in progress no premature beat follows; the ventricle makes no response to the stimulus at all. This period during which the ventricle is insensible to stimuli, is called the "refractory" period. The result is that when a succession of stimuli repeated at a given rate are sent into the ventricle, the number of beats does not correspond to the number of stimuli; some of the stimuli falling into refractory periods are ineffective and produce no beat. Hence the impossibility of producing tetanus of the heart by means of rapidly repeated stimuli, the usual effect of which is to throw the heart into the condition of incoordinated contraction known as fibrillary contraction or heart delirium. When a premature extracontraction of the ventricles of an entire heart, which is beating regularly, is induced by sending an intercurrent stimulus in during the diastole, this contraction will be larger, the later the stimulus is thrown in. After this contraction a longer pause than usual follows, the "compensatory" pause and so the regular sequence between the auricles and ventricles is reestablished (Fig. 736).

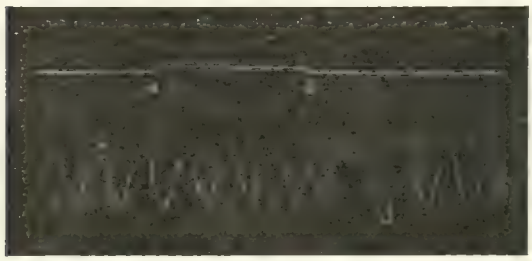

FIG. 736.—Direct Stimulation of the Isolated Heart of the Cat. (According to Langendorff.) To be read from left to right; systole is represented by the down-stroke. The stimulus thrown in at *a*, beginning of systole, remains ineffective; stimulation at *b*, middle of diastole, causes an extracontraction. The compensatory pause and the increased contraction following it are also shown.

Sequence of the Beat.—The beat of the heart normally begins at the venous end and sweeps over the organ to finish at the arterial end. The myogenic theory must provide a plausible explanation for the origin of the beat at one point and its propagation in one direction over the heart. In cold-blooded animals as well as in mammals (Kent) there is direct muscular continuity between the several segments of the heart, so that anatomically there is no difficulty in assuming the propagation of the contraction wave from muscle fiber to muscle fiber through the entire length of the organ. Measurements of the rate at which the contraction wave advances have been made; but the results hardly afford conclusive evidence in favor of muscular conductivity. The probability of muscular conduction of the excitation wave through the heart is shown, however, in a number of significant observations. The auricle may be slit by a series of interdigitating cuts and a contraction wave starting from the sinus will travel around the ends of the several sections until, arriving at the ventricle, will cause contraction of that chamber. Propagation over nerve trunks in this case is evidently excluded. The reversed sequence observed in mechanical stimulation of the ventricle in a quiescent heart also supports the theory of muscular conduction. No conceivable arrangement of a definite nervous mechanism constructed in accordance with the neurone doctrine seems capable of explaining this fact. It remains only to inquire why the beat begins at the venous end. It was shown above, in connection with the neurogenic theory, that the potentiality of beating was greater in the sinus of the frog's heart than in the other parts. The isolated ventricle, when it beats at all, does so with a slower rhythm than the sinus. Similarly it can be shown on the terrapin's heart that interference with the muscular substance of the auricle, when carried to a certain extent, prevents the beat of the auricle from passing over to the ventricle so that the sequence is broken after the auricle beat. If, for instance, the auricle be cut through until only a narrow bridge of muscle is left connecting the sinus end with the ventricular end of the heart, or if the auricle be compressed with a clamp, a point may be reached in which every second or every third beat only of the sinus is followed by a beat of the ventricle. Then if the bridge be still further narrowed or the clamp tightened, the ventricle stops altogether, or it may after a while set up an independent rhythm of its own, slower than that of the sinus. Experiments upon isolated strips taken from the sinus, auricle, and ventricle of the turtle's heart respectively show that the concentration of salts in the blood is adjusted to the irritability of the venous end. Sinus strips begin to beat at once in solutions of that degree of concentration; ventricular strips remain quiescent until the concentration is altered to suit their peculiar state of irritability. The normal sequence, therefore, is merely the result of the fact that the normal stimulus of the heart is attuned, so to speak, to the physiological properties of the venous end; the beat once inaugurated travels along from fiber to fiber until the cycle is completed. And so the auricle, as has been stated before, becomes the pacemaker of the entire heart and an important regulator of its work. The pause observed between the contractions of the auricles and ventricles is the result of the retardation of the excitation wave in its propagation through the slender and peculiar auriculoventricular bundle; the condition is similar to that produced artificially by restricting the conducting muscular tissue by appropriate sections or by the clamp as described above. The interference with the conduction process is therefore spoken of as a "block." Cases of complete or partial heart block have been observed in man in the condition known as the Stokes-Adams syndrome. By comparing the arterial and venous pulse rates it is possible to determine whether the block is partial or complete. In the former case a definite ratio between the two is observed, the ventricle beating after every second or third auricular systole; but where the block is complete the rhythm of the ventricles is slow and entirely independent of that of the auricles. The pathological findings in a number of these cases show a lesion involving the auriculoventricular bundle. Evidently each chamber has a rhythm of its own but the rhythm of the auricles being more rapid than that of the ventricles will determine the rhythm of the whole heart so long as the physiological connection between the two remains intact.

2. *The Extrinsic Nerves of the Heart.*—While the heart contains within itself all the conditions necessary to the development of a regular rhythmical beat, its activity is constantly controlled and modified by impulses coming to it through the extrinsic cardiac nerves. It has already been stated that these nerves are derived from two sources, one set of fibers arising from the medulla and passing through the vagus nerves, the other set arising from the upper thoracic portion of the spinal cord and reaching the heart by way of the sympathetic chain. The general course of both sets of fibers is sufficiently set forth in the diagram of the cardiac nerves of the dog (Fig. 737).

(*a*) The Inhibitory Nerves of the Heart.—The Weber brothers discovered in 1845 that stimulation of the peripheral stump of the divided vagus nerve with the faradic current caused either a slowing or complete cessation of the heart beat according to the intensity of the stimulus; that the vagus in

other words contains inhibitory fibers for the heart. Section of both nerves they found to be followed by an acceleration of the pulse, the effect being more pronounced in animals of slow pulse. The inhibitory action of the vagus on the heart is conveniently demonstrated upon a blood-pressure record, in which the altered heart rhythm as well as its influence on the height of arterial pressure in immediately apparent (Fig. 738). The slowing of the beat is, however, not the only effect of vagus stimulation on the heart. The force and extent of the individual beats are also diminished, and the effects upon the rate and force are to a certain extent independent of one another, so that in a given case the rate may remain entirely unchanged while the contractions go on diminishing in extent and force until complete arrest results. The contrary effect of a slowing in rate without simultaneous diminution in size is not known to occur. Finally stimulation of the vagus produces a partial or complete loss of tone, thus allowing more complete relaxation and giving rise to the characteristic overdistended and engorged appearance of the completely inhibited heart. The inhibition from vagus stimulation tells much more on the auricles than on the ventricles, the extent of the auricular contraction being especially affected. The auricles may be brought to a complete standstill while the ventricles continue to beat, the latter then exhibiting that independent rhythm spoken of above. In a somewhat similar manner the stimulation of the vagi, by affecting the rhythm of the auricles more than that of the ventricles may lead to a lack of coordination between the two, the specially slowed auricles beating at one rate, the ventricles at another. The question as to whether the vagus acts directly on the ventricles, as it does on the auricles, or whether the effect on them is of a secondary nature caused by the changes in the auricle must for the present be left undecided.

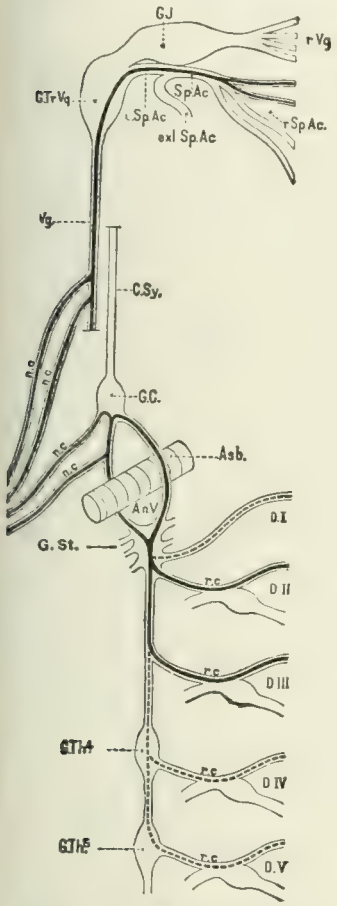

FIG. 737.—Diagrammatic Representation of the Cardiac Inhibitory and Augmentor Fibers in the Dog. The upper portion of the figure represents the inhibitory, the lower the augmentor fibers.

(*b*) Accelerator Nerves.—Diametrically opposite changes are set up in the heart on stimulating the peripheral end of one of the accelerator nerves. These nerves are characterized by their lesser irritability, a longer latent period of stimulation and a more lasting after-effect when compared with the pneumogastrics. With a suitable stimulus an acceleration of the heart amounting to from five to one hundred per cent. may be obtained according to the initial rate at which the heart is beating. As in the case of the inhibitory fibers, the effect is of a dual nature, the increase in rate being generally accompanied by an increase in the size and force of both auricular and ventricular contractions. Either effect may. moreover, appear alone, so that the name "augmentor" has come to be used side by side with that of "accelerator" for these nerves. In fact, the suggestion has been offered that the heart really receives four distinct varieties of nerve fibers through its extrinsic nerves instead of two, corresponding to the several results obtained by artificial stimulation, namely, accelerating, retarding, augmenting, and depressing fibers. It is interesting to note the effect of simultaneous stimulation of both inhibitory and accelerator nerves. It was long believed that even feeble stimulation of the vagi was able to overcome comparatively strong stimulation of the accelerators, so that when both

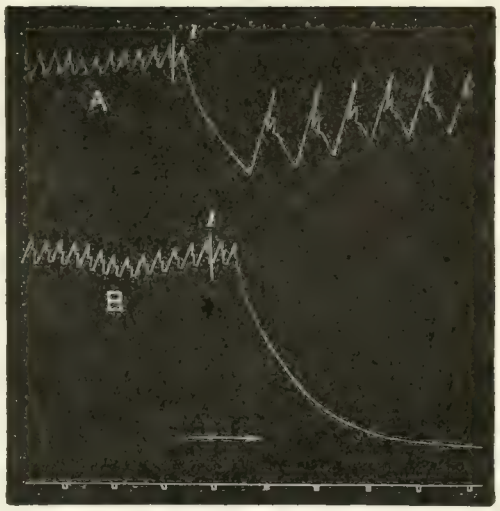

FIG. 738.—Blood-pressure Tracing (Rabbit). Vagus stimulated at *I*. Stimulus stronger in *B* than in *A* (Hürthle's spring manometer).

nerves were stimulated together the inhibitory effect predominated so long as the stimulus lasted. Upon the cessation of the latter, however, the characteristic accelerator after-effect showed itself in a secondary quickening of the heart, indicating that the effect of the stimulus on the accelerator nerves was only temporarily superseded. Later experiments have shown that these two sets of nerves are true antagonists, and that the effect of simultaneous stimulation is determined entirely by the relative strength of the stimuli applied to them. Hunt concludes that in all cases the result is approximately the algebraic sum of the results of stimulating them separately. The mechanism through which these nerves produce their characteristic effects upon the heart, and the nature of the ultimate changes underlying the inhibition and acceleration, are also points of fundamental theoretical importance. As to the first part, it has been supposed that some of the intrinsic ganglia of the heart constitute peripheral nervous mechanisms which mediate between the extrinsic nerves and the heart muscle. Reasons have already been given for denying to these ganglia any share in the maintenance of the normal beat, and hence the suggestion that they may act as local inhibitory and local augmentor centers. The evidence adduced in support of this view is based on the action of certain heart drugs, such as nicotine, atropine, and muscarine, and on the interesting

classical experiments known as the "ligatures of Stannius." Since neither of these series of experiments is thoroughly understood and both admit of various equally plausible explanations, they have furnished no crucial test or definitive solution of the problem. In fact it may be said that no clear evidence has been obtained to show that the nerve cells within the heart in any essential manner modify the physiological impulses falling into them and so affect their ultimate results. The action of both inhibitory and accelerator fibers must be direct upon the muscular tissue itself and this leads to the second part of the question as to the ultimate nature of these effects. It has been suggested by Gaskell that the sympathetic fibers by their augmentor and accelerator impulses increase functional activity by exciting catabolic changes, and that the inhibitory effect of the vagus fibers is the result of anabolic changes set up by the impulses they transmit. According to this theory the natural effect of inhibition should be increased power and efficiency; that of acceleration, lessened efficiency, fatigue, or exhaustion. Experiment shows that this is exactly what occurs. The activity of a weak heart has frequently been heightened by vagus stimulation, while a fairly vigorous heart, especially a bloodless one, may by repeated stimulation of the accelerator fibers be reduced to a feeble condition. In support of the view that the changes set up in the heart by vagus stimulation are of a constructive anabolic kind must be mentioned the positive variation of the demarcation current which accompanies such stimulation. If the ordinary conception that the negative variation accompanying functional activity in various tissues is an indication of increased catabolism be accepted, it is fair to infer from a positive variation that changes of an opposite character are going on. But the clearest proof of the trophic nutritive influence of the vagus on the heart is obtained from the study of the pathological changes appearing in that organ as a result of unilateral vagotomy in animals. All other organs remain normal while the heart alone presents an area of atrophic degeneration varying in position according to which nerve was cut (Fantino).

A more specific theory has been proposed recently by Howell to explain the inhibitory action of the pneumogastrics on the heart. Cardiac muscle is known to contain a large percentage of potassium salts in combination; during vagus stimulation Howell finds that potassium in diffusible form is given off from the auricular musculature. His theory assumes that the vagus impulses initiate the dissociation or decomposition which sets free the potassium and by the resulting increased concentration of potassium ions slow or stop the heart. As to the normal mode of functioning of these two sets of antagonistic nerves, it is to be noted in the first place that both are in a state of tonic activity; section of both vagi causes a marked acceleration, while subsequent destruction of the accelerators distinctly slows the rate again. The origin of this continuous activity is at the centers, and a change in the rate of the heart in either direction may evidently be brought about in two ways, by increasing or diminishing the activity of either of these centers. Nature seems to provide here an excess of regulating mechanism with superfluous extravagance, but the general occurrence of this double mechanism throughout the series of vertebrate animals, and even among certain invertebrates, indicates that some useful end must be gained by this arrangement; possibly greater promptness and accuracy of response to regulating influences controlling this important central organ. In other parts of the body, where smooth and prompt reactions are required, similar balanced mechanisms are found, as for example, in the iris with its constrictor and dilator muscles, and in the flexor and extensor muscles of the joints with their reciprocal innervation. The inhibitory and accelerator nerves are subject to stimulation along their course to the heart only under very exceptional circumstances, as by a tumor or an aneurysm pressing upon the nerve trunks. The impulses which regulate the activity of the heart are normally discharged from the centers which lie in the medulla oblongata. While there is no satisfactory evidence to indicate the existence of automatic activity in these centers, various conditions are known to modify their activity, and practically every afferent nerve of the body comes into reflex relation with them. The medullary centers of the cardiac nerves are well known to be influenced by the higher brain centers. Various psychical states, such as pleasure, pain, hope and fear, may quicken or slow the heart and occasionally individuals are able by voluntary effort markedly to accelerate the pulse. The state of the blood-pressure also modifies the activity of these centers. An isolated heart does not react by change of rate to variations of either arterial or venous pressures within physiological limits; but in the body with its nerve connections intact it may almost be put in the form of a law, that "the rate of the beat is in inverse ratio to the arterial pressure"; a rise of pressure being accompanied by a diminution and a fall of pressure by an increase of the rate. When the vagi are divided, this relation is no longer observed, hence it is inferred that increased pressure causes a slowing of the beat, when the vagi are intact, because the inhibitory center is stimulated by the high pressure, either directly by the pressure obtaining in the blood-vessels of the medulla, or in some indirect manner, and the heart in consequence is more or less inhibited. The afferent impulses, which reflexly modify the activity of the medullary center, arise everywhere in the body, including the heart itself, and only a few special cases need be referred to here. The heart is supplied with centripetal nerves which normally mediate certain unconscious reflexes and under pathological conditions may produce painful sensations. Wooldridge described fibers on the anterior and posterior surfaces of the ventricle, stimulation of whose central end gave either reflex acceleration or inhibition. The depressor nerve of Cyon, which will be referred to in more detail later, also takes its origin in the heart and reflexly inhibits it when the central end is stimulated, the vagi being intact. Reflex inhibition results also from the stimulation of the following nerves: the central end of either vagus, the other being intact; the superior laryngeal nerve; the splanchnic, and the trigeminal. Reflex acceleration is obtained by forcible inflation of the lungs, and in man whenever intrapulmonary pressure is increased, as in loud talking, singing, etc. Sensory nerves in general give either inhibition or acceleration, the result apparently depending in part at least on the intensity of the stimulus; feeble stimulation giving acceleration, strong stimulation inhibition. In the normal and pathological changes of the heart rate of reflex origin, it is rarely possible to interpret the result in terms of the mechanism involved. Slowing and quickening of the beat may be produced through either center, since both are in tonic activity. The older physiologists attributed the main share of the reflex regulation of the heart to the cardioinhibitory center, but with accumulating experimental evidence, the equal significance of the accelerator mechanism is receiving fuller recognition.

Vasomotor Nerves.—From what has been said about the influence of gravity and the respiratory movements on the blood flow in the veins, it is clear that these mechanical factors influence the distribution of the blood in the body more especially that in the veins. Aside from such changes, however, the vascularity of the various organs undergoes incessant fluctuations, which are evidently correlated in part

with changes in their functional activity and in part related to the heat regulation of the body. These changes in blood supply are not the passive effects of mechanical factors like those just mentioned, but are brought about by local changes in the walls of the vessels themselves, especially those of the small arteries, by which their caliber is increased or diminished; and these changes throughout the body are so coordinated that in general it may be said that the blood flow to each organ is constantly adapted to the existing state of its physiological activity. By holding the ear of a rabbit up before the light or watching the web of a frog's foot under the microscope, such changes in the caliber of the arteries may be readily seen. It will be noticed that these vessels frequently expand and contract without any apparent cause, rarely remaining at rest for any great length of time. The size of the vessels thus oscillates about a mean state of moderate contraction, which is permanent though variable and which is spoken of as their tone or tonicity. The arteries owe this tone to the peculiar properties of the non-striated involuntary muscle tissue which enters so largely into the structure of their walls, forming as it does practically the whole thickness of the middle coat in the smaller arteries, where the changes in question are most marked. Histological examination shows, moreover, that these muscle fibers are richly supplied with nerves by which their activity is regulated and controlled, and to which therefore the name of vasomotor nerves has been given. The study of the vasomotor nerves becomes of paramount importance in view of the intimate relations they bear to the activity of every organ and tissue of the body. The fact that the apparently spontaneous irregularly rhythmical changes in caliber of the arteries are under the control of special vasomotor nerves was discovered by Cl. Bernard in 1851 when he divided the cervical sympathetic nerve in the rabbit. He observed as the result of this operation that the vessels of the ear on the same side visibly expanded, small arteries and veins standing out distinctly which before could not be recognized. The temperature of the ear rose, and from a divided vein blood of a bright hue flowed in a rapid stream. The spontaneous changes of caliber had disappeared. On stimulating the head end of the divided nerve, the arteries again contracted, the venous outflow diminished, and the temperature of the ear fell. Nerves which thus bring about contraction of the vessels when stimulated are called "vasoconstrictor" nerves, and the experiment cited above shows that the vasoconstrictors distributed to the rabbit's ear are in tonic activity so long as their normal connection with the central nervous system remains intact.

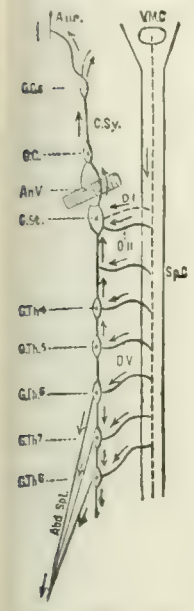

Fig. 739.—Diagram Illustrating the Paths of Vasoconstrictor Fibers along the Cervical Sympathetic and (Part of) the Abdominal Splanchnic. *Aur.*, Artery of ear; *G.C.s.*, superior cervical ganglion; *Abd.Spl.*, upper roots of and part of the abdominal splanchnic nerve; *V.M.C.*, vasomotor center in spinal bulb; *C.Sy.*, cervical sympathetic; *G.C.*, lower cervical ganglion; *An.V.*, annulus of Vieussens; *G.St.*, stellate ganglion; *G.Th.*^{4}, *G.Th.*^{5}, *G.Th.*^{6}, *G.Th.*^{7}, *G.Th.*^{8}, thoracic ganglia; *D.I*, *D.II*, *D.V*, thoracic spinal nerves. The paths of the constrictor fibers are shown by the arrows. The dotted line along the middle of the spinal cord, *Sp.C.*, is to indicate the passage of constrictor impulses down the cord from the vasomotor center in the spinal bulb.

Since the time of Bernard's classical experiment the distribution of nerves of similar function to nearly every vascular area of the body has been demonstrated and their anatomical course traced out. In general their path is much the same for all the mammals, and may be briefly described as follows (Fig. 739). Leaving the spinal cord in the anterior roots of the nerves belonging to the middle region, say from the second thoracic to the fourth lumbar nerve, they pass by the visceral branches to the corresponding thoracic and abdominal sympathetic ganglia. Those destined for the head and neck emerge chiefly in the second and third thoracic nerves, turn upward in the sympathetic chain to pass by way of the annulus of Vieussens, lower cervical ganglion, and cervical sympathetic nerve to the superior cervical ganglion. The axones of the spinal efferent neurones terminate here about the cells of the ganglion and the path of conduction is continued over sympathetic neurones whose axones extend to the blood-vessels by way of numerous branches arising from the ganglion. For superficial organs the connection in general leads through sympathetic branches to the cranial nerves; for deep structures, the sympathetic nerves running in the coats of the corresponding arteries furnish the anatomical path. The vasoconstrictor fibers for the abdominal viscera passing through the sympathetic main chain without interruption, enter the splanchnic nerves and arborize about cells in the prevertebral ganglia of the great nerve plexuses of the body cavity. The fibers which are intended for the extremities and trunk, after a longer or shorter course along the sympathetic chain within whose ganglia cell connection is made, return in the gray rami communicantes to the spinal nerves, and so reach the brachial plexus, the sciatic plexus, or other spinal nerve, as the case may be to pass out to their appropriate areas of distribution. The vasoconstrictor nerves as they leave the cord are of the fine medullated variety; they connect in every case with a sympathetic cell, situated either in a vertebral or a prevertebral ganglion, as shown by Langley's nicotine reaction, and are designated therefore as "preganglionic" fibers to distinguish them from the axones of the sympathetic neurones. The latter as non-medullated fibers complete the path to the blood-vessel and constitute the "postganglionic" fibers. There seems to be no exception to this general plan of arrangement and distribution of the vasoconstrictor nerves. The vagi have been investigated with reference to the possibility of a vasomotor function especially in connection with the coronary arteries. But the evidence in this case is conflicting and inconclusive. The apparent exception presented by the auricularis magnus, a branch of the third cervical nerve has been shown to conform to the rule. The vasoconstrictor fibers supplied by this nerve to the blood-vessels of the ear in the rabbit do not emerge from the cord in the roots of the third cervical nerve but in the general outflow from the thoracic region. They reach the third cervical through gray rami communicantes from the first thoracic ganglion which makes similar connections with a number of cervical nerves.

Another type of vasomotor nerve is represented in the fibers supplied by the lingual nerve to the submaxillary gland and adjacent structures (Fig. 740). When these fibers are divided no vascular effect is observed; but on stimulating their peripheral ends the vessels of the gland are seen to dilate and swell and the blood gushes from the efferent veins with a distinct pulse and a bright arterial color. This class of fibers designated "vasodilator" nerves, is not in tonic activity like the vasoconstrictors and their influence can be exerted in one direction only, viz., to dilate the blood-vessels. The vasodilators have also been shown to be widely distributed and possibly occur wherever the vasoconstrictors are found. The demonstration of the vasodilator fibers when they occur alone as in the lingual nerve or in the nervi

erigentes is not difficult, but when they are combined in the same nerve trunk with vasoconstrictor fibers as is usually the case, special devices must be used to show their presence. Simultaneous stimulation of both kinds of fibers generally produces vasoconstriction although marked dilatation may appear as the after-effect.

The vasodilators differ from the constrictors physiologically in several ways. When stimulated, the

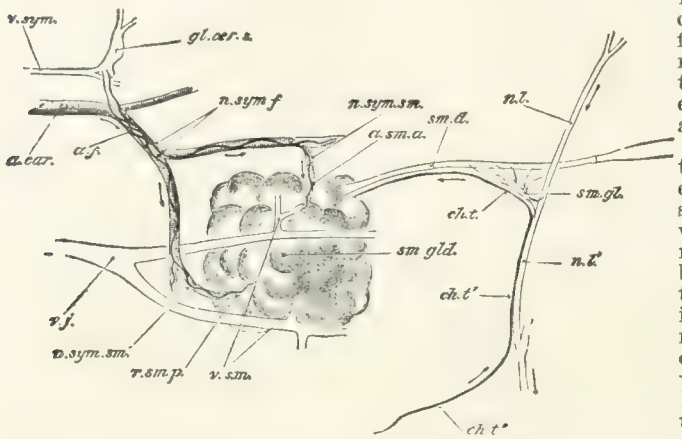

Fig. 740.—Diagrammatic Representation of the Submaxillary Gland of the Dog with Its Nerve and Blood-Vessels. *sm.gld.*, The submaxillary gland, into the duct (*sm.d.*) of which a cannula has been tied. The sublingual gland and duct are not shown. *n.l.*, *n.l'*, the lingual branch of the fifth nerve, the part *n.l.* is going to the tongue; *ch.t.*, *ch.t'*, *ch.t''*, the chorda tympani. The part *ch.t''* is proceeding from the facial nerve; at *ch.t'* it becomes conjoined with the lingual *n.l'* and afterward diverging passes as *ch.t.* to the gland along the duct. The continuation of the nerve in company with the lingual *n.l.* is not shown. *sm.gl.*, the submaxillary ganglion with its several roots; *a.car.*, the cartoid artery, two small branches of which, *a.sm.a.* and *v.sm.p.*, pass to the anterior and posterior parts of the gland; *v.s.m.*, the anterior and posterior veins from the gland, falling into *v.j.*, the jugular vein; *v.sym.*, the conjoined vagus and sympathetic trunks; *gl.cer.s.*, the upper cervical ganglion, two branches of which, forming a plexus (*a.f.*) over the facial artery, are distributed (*n.sym.m.*) along the two glandular arteries to the anterior and posterior portions of the gland.

latent period seems somewhat longer, the effect reaches a maximum more slowly and it persists much longer. Their irritability is also of a different kind, disappearing more slowly after section of the nerve or on cooling and making them more sensitive to weak, slowly repeated stimuli (Fig. 741). These differences furnish the means of tracing these nerves even in the mixed trunks and of determining their anatomical paths. Many of them follow the same anatomical course as the vasoconstrictors. These include the vasodilators to the trunk and extremities, to the visceral structures in the body cavity and to certain regions of the face and buccal cavity. All of these issue from the cord in the anterior roots of the lower cervical, thoracic, and upper lumbar spinal nerves and pass in their course outward through the sympathetic system in essentially the same way as the constrictor fibers. There are special groups, however, which run a different course. There is a cranial outflow in the facial and glossopharyngeal nerves for the blood-vessels of the salivary glands, tongue, tonsils, soft palate, pharynx, and adjacent structures and possibly in the vagus for the coronary arteries. A special group of vasodilators also arises from the sacral region of the cord in the anterior roots of the first, second, and third sacral spinal nerves. These are distributed through the nervi erigentes and hypogastric plexus to the vessels of the external genital organs. In these instances the vasodilator fibers, as they leave the central nervous system, are like the vasoconstrictors, fine, medullated nerves; but they do not pass through the sympathetic chain and retain their medulla for the greater part of their course, losing it only near their final termination in the tissue whose blood-vessels they supply. The sympathetic cells with which they connect and which supply the postganglionic fibers in these special groups, lie in the small peripheral or terminal ganglia. It may be mentioned also as a curious anomaly that some of the vasodilator fibers leave the spinal cord in a number of the posterior roots. First discovered in the lumbar region (Stricker, Morat), they have recently been shown to occur in the posterior roots of the fourth, fifth, sixth, and seventh lumbar and first sacral nerves for the posterior extremity, and also in the roots of the cervical and brachial plexuses, especially the seventh cervical and first thoracic, for the anterior extremity.

Venomotor Nerves.—The statements made thus far concerning vasomotor nerves apply entirely to the arterial portion of the vascular system. Now the veins are also provided with muscular fibers and contain plexuses of nerve fibers in their walls. It has, moreover, been known for a long time that they contract in response to various stimuli, and that in certain cases, as in the wing of the bat, rhythmical contractions occur. Physiological experiment has shown more recently that the veins possess true vasomotor nerves. In 1892 Mall demonstrated the vasoconstrictor fibers to the portal vein in the splanchnic nerve and showed that through their stimulation as much as twenty-seven per cent. of the total blood could be displaced from the splanchnic area and driven forward to the right side of the heart. Since that time, similar fibers have been traced for the veins of the hind limb and their general course and arrangement found to correspond to that of the arterial vasomotor fibers to that limb. In this connection it may be interesting to refer to the observations of Bert and Laffont in 1882 and the more recent work of Camus and Gley, according to which the receptaculum chyli and thoracic duct both receive dilator and constrictor fibers through the thoracic sympathetic chain and splanchnic nerves. It seems plausible to conjecture that the distribution of these two kinds of fibers may be general to all parts of the vascular system.

As to the mechanism through which the vasomotor nerves influence the caliber of the vessels,

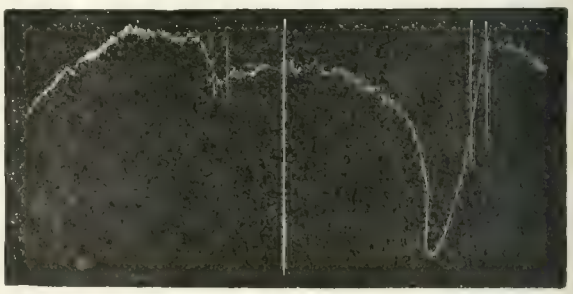

Fig. 741.—Plethysmograms (Hind Limb of Cat). To be read from right to left. On the left hand is shown the effect of slow stimulation of the sciatic (1 per second); on the right hand the effect of rapid stimulation (64 per second).

little can be said. The constrictor fibers represent the motor fibers, whose impulses increase the tone or degree of contraction of the involuntary muscle tissue in the coats of the vessels, while the removal of constrictor influences previously exerted is followed by a passive dilatation under the influence of the blood pressure from within. The dilator nerves

are usually compared to the inhibitory fibers of the heart and the dilatation which they produce is considered a passive one. It has been maintained, however, that they cause an active dilatation of the vessels which is independent of the pressure within, and in support of this view there are on record some interesting observations on the frog's tongue by Frey (1876), which have been recently repeated and perfected by Siawcillo. According to these observers an active expansion of the smallest arteries and capillaries made sufficient suction to start a current in the vessels after the blood had come to absolute rest under a uniform zero pressure.

Vasomotor Centers.—The vasodilator nerves, characterized by the absence of tone, are apparently called into play only occasionally as parts of a reflex mechanism. The centers from which they arise lie widely separated in different regions of the central nervous system. Thus the reflex center for the fibers descending in the chorda tympani lies in the medulla oblongata, while the center of origin of the fibers in the nervi erigentes is placed in the lower part of the cord; and in general the center for each group may be said to lie in the central nervous system, not far from the superficial origin of the nerves in which the vasodilator fibers run. The vasoconstrictor nerves are on the contrary under the control of a general center situated in the medulla, occupying a region which extends from a point four to five millimeters above the point of the calamus scriptorius to within one to two millimeters of the corpora quadrigemina. This center is in continued tonic activity, so that section of the cord below the medulla results in a general loss of tone throughout the vascular system and a great fall of blood pressure. The existence of a presiding center confers upon the constrictor mechanism the power of producing general effects, and its utility is further increased by reason of its tonic activity, since the same fibers may by an increase in the impulses passing along them be the means of constriction and by the removal or diminution of the tonic influence be the means of dilatation. When an animal whose cord has been divided in the thoracic region is kept in good condition, the arteries of the hind limbs and hinder part of the body which became dilated at the time of the section after a while reestablish a normal or nearly normal tone. This and the fact that they undergo reflex changes of caliber indicate that there are other centers for the vasoconstrictor nerves scattered along the spinal cord. These centers seem to be less irritable than the medullary center under whose control they normally stand, but their great power of endurance would indicate that they may play an important rôle in maintaining a normal vascular tone. Finally, experiment has shown that the vessels may slowly recover their tone after extirpation of the entire spinal cord. They are at first completely paralyzed and maximally distended; gradually, however, their tone returns and they begin to react to local applications of heat or cold much as they do under normal conditions. It follows that the vessel walls themselves possess the power of exhibiting independent tonic contractility, or else this recovery indicates the existence of vasomotor centers of a third order in the peripheral ganglia distributed along the course of the nerve trunks. Such a tone of peripheral origin would explain the additional dilatation observed on stimulating vasodilator nerves to parts whose vasoconstrictor nerves had previously been divided. From what has been said it follows that the simplest efferent path along which the vasomotor impulses can pass may be considered as built up of two neurones, one with its cell body in the central nervous system and the other in a sympathetic ganglion. Since, however, the spinal vasomotor centers are under the control of the chief center in the medulla, the axis-cylinder processes of the cells of the bulbar center must come into relation with the spinal vasomotor cells, and so the complete efferent path comes to include three nerve units.

Vasomotor Reflexes.—The activity of the centers in the medulla and cord from which the vasoconstrictor and vasodilator fibers take their origin is determined in large measure by the impulses falling into them along various afferent nerve channels giving rise to reflex vasomotion. The possible afferent paths include practically every centripetal nerve in the body, those distributed to the vessel walls not excepted; while the response may vary from a slight local effect in the region whence the afferent impulse started to a change involving an extensive vascular area sufficient to produce variations in the general blood pressure. The local reflexes, such as the congestion of the skin on the application of warmth, are commonly dilatations, although constrictions also occasionally result. Of the general reflexes those occurring in the great splanchnic area are perhaps the most frequent, sensory stimulation causing constriction there with special ease. Stimulation of sensory nerves may, however, cause reflex dilatation in the splanchnic region, while in the vessels of the skeletal muscles this is the rule. In them the reaction affects first the muscles which stand in a more or less intimate functional relation with the stimulated nerve, but it may become general and so become an efficient means of bringing on a general fall of blood pressure. It is apparent that the effect on the blood pressure of stimulating a sensory nerve will depend on the relative extent of the antagonistic changes, both of which are usually present, and the question as to

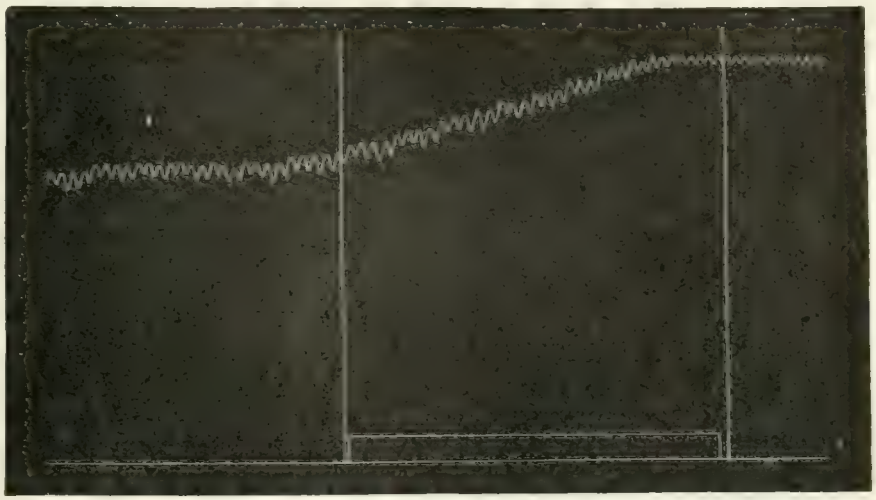

Fig. 742.—Blood-pressure during Electrical Stimulation of the Depressor Nerve. To be read from right to left. The time of stimulation is indicated by the vertical lines (— = 10 seconds).

the conditions which determine the preponderance of vasodilatation in one case and of vasoconstriction in another is one of unusual interest. We know at present but one nerve, the so-called depressor nerve of Cyon, whose stimulation regularly brings on a fall of blood pressure (Fig. 742). This is the sensory nerve of the heart which has already been referred to as causing reflex inhibition of the heart. The effect on blood pressure is not dependent on this heart action, as it still occurs after section of both vagi, but is due to an extensive vasodilatation in which the splanchnic area has a prominent share, although the vessels of other parts of the body also participate. The dilatation appears to be due to an inhibition or depression of the tonic activity of the vasoconstrictor center, since the effect is diminished or abolished by agencies which reduce or destroy the irritability of this center, and hence the name of "depressor" for this nerve. Since sensory nerves in general produce both kinds of effect, "pressor" and "depressor" the question arose as to whether they contain two distinct varieties of nerve fibers or whether the different results depend only on the condition of the centers and the character of the stimuli used. That both of these factors may influence the result can be easily shown. A sensory nerve like the sciatic, whose stimulation regularly produces vasoconstriction and rise of blood pressure in an animal under curare (Fig. 743) will frequently give a fall of pressure when chloral or ether is used for the anesthetic. Again, mechanical stimulation of the sensory nerves in muscles by kneading or massage regularly causes reflex vasodilatation, while electrical stimulation of the same nerves gives reflex constriction. On the other hand there is strong evidence for the view that there are both "pressor" and "depressor" or "reflex vasodilator" fibers in the sciatic and other peripheral trunks. The pressor fibers ordinarily have the upper hand, but by subjecting the nerve to the action of cold or stimulating

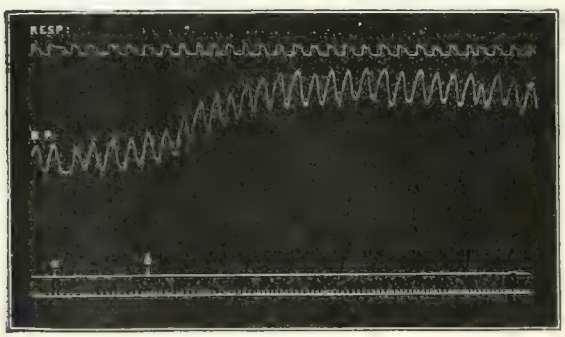

Fig. 743.—Pressor Effect Produced by Stimulating the Central End of the Sciatic of a Curarized Cat Under Morphine. Time tracing in seconds. Reduced one-half.

the nerve at a certain stage of regeneration after section, the depressor effect may be obtained. The depressor fibers seem to retain their power of conduction longer than do the pressor fibers when cooled, and when the nerve is cut and sutured they regenerate earlier. There is also a certain amount of evidence to indicate that the fall of pressure from stimulation of the sciatic and similar nerves is of a different nature from that resulting from stimulation of the depressor nerve of the heart (Fig. 744). In the former case the dilatation occurs largely in the limbs and is probably due to a reflex stimulation of dilator fibers, so that the name "reflex vasodilators" has been suggested for this class of fibers to distinguish them from the "depressor" fibers proper which act by inhibiting the vasoconstrictor center. The complicated nervous mechanisms associated with the circulatory apparatus enable the nervous system, directed by afferent impulses which reach it along various channels, to coordinate the action of the heart and vessels and to direct the blood flow according to the needs of the body. The blood-supply of the organs is continually shifting according to their varying activity; but dilatation and increased blood flow to the active organs is met by compensatory constriction elsewhere, thus preventing a wasteful use of cardiac energy which would otherwise be required to keep up the general

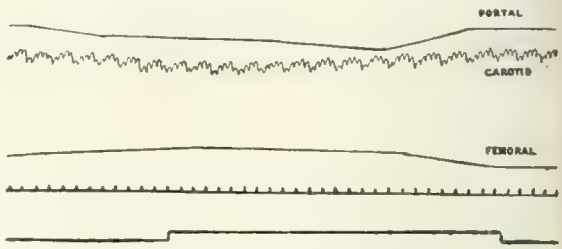

Fig. 744.—Dog. Ether. Vagi intact. Fall of pressure in carotid and portal vein, and rise in femoral vein on stimulation of sciatic at 10°. All the curves have the same base line; the curves of venous pressure being drawn to indicate the pressure in millimeters Na_2CO_3, the curve of arterial pressure in millimeters Hg. The changes of pressure in the curves must be multiplied by two to obtain the absolute changes. Tracing from right to left.

blood pressure. This reciprocal relation is particularly conspicuous between the blood-vessels of the somatic and those of the splanchnic divisions of the body, thereby providing the chief means by which the blood pressure is regulated and by which the maintenance of a normal body temperature is in large measure secured. George P. Dreyer.

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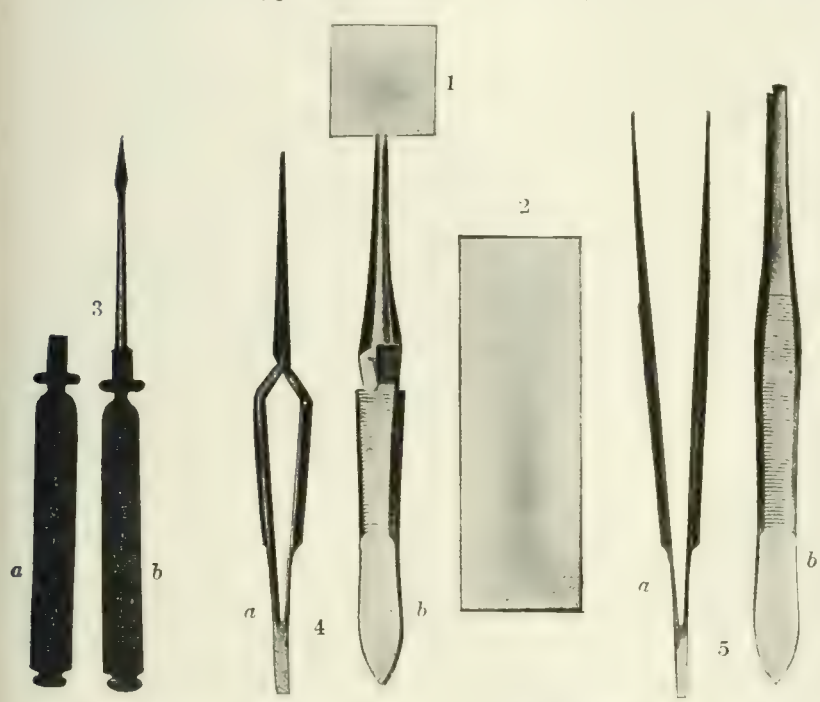

Fig. 745.—1, Bausch and Lomb, $\frac{3}{4}$ inch, No. 1 cover slip; 2, Bausch and Lomb, extra thin slide; 3, blood sticker, two views—*a*, point in sheath for carrying instrument in pocket; *b*, point in place ready for use; 4, clamp forceps, two views—side view, showing close apposition of tip of limbs; front view, showing proper extent of grasp of cover slip (1); 5, open forceps, two views—side view, front view. (Instruments made by F. Arnold & Son, Baltimore, Md.)

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Note.—The tables which appear in this article give the blood characteristics of the diseases detected by blood examination. Beyond this no clinical description of the disease is given. Certain blood examinations, as the iron content of the blood, "iodophilia," specific gravity of the serum, have been omitted as not suitable for clinical application. Agglutination, hemolysis, morphological and cultural characteristics of bacteria and parasites of the blood, the detection of occult blood, and blood stains will be found in this Handbook under appropriate heads, consideration of these subjects not appearing in this article.

I. Fresh-blood Specimen.

Apparatus and Technique.—In preparing the blood for microscopic examination, however careful the technique employed, the operator is subjecting one of the most delicate tissues of the body to very rough and unnatural surroundings. When one realizes the exquisite smoothness of the intima of the blood-vessels, the wonderfully regulated temperature of the body, the delicate structure of the red cell, the even more delicate structure of the plate which without most careful preservation is entirely destroyed a few seconds after exposure to the air—when one realizes all these factors it is surprising that any technique is delicate enough to enable one to obtain a specimen in which the corpuscles retain even approximately their normal and pathological characteristics. This realization at the same time emphasizes the importance of observing every precaution which experience has shown to be necessary in the preparation of the blood specimen which shall be, outside of the body, as nearly as possible representative of the blood as it appears in the circulation.

The object then of apparatus and technique is to produce surroundings as nearly like those normal to the blood in circulation as possible. To accomplish this we must observe the following: (1) Absolute cleanliness and freedom from moisture; (2) avoid chilling the blood; (3) avoid exposure to air; (4) avoid rough treatment of the drops and consequently of the constituents thereof—the corpuscles.

Since this article (now largely rewritten) originally appeared practically every hospital has acquired a

clinical laboratory and accurate technique in blood work is quite universal, yet the failures in blood work in hospitals are due, in the large majority of instances, to not observing the precautions just enumerated. The writer therefore wishes to state that in the technique here recommended nothing is advocated that has not been proven to be essential in order that a hospital laboratory shall produce *reliable* and *uniform results*.

It is not difficult for even beginners to observe pathological changes in a well-taken specimen of blood under the microscope, while a specimen carelessly taken presents difficulties to an expert. Not infrequently, after attempting to form an opinion from a poor specimen offered by an interne, we have taken another specimen and the interne himself has promptly observed the important diagnostic features. Such poor specimens frequently result from the "slide," "cigarette paper," and other coarse, short cut methods, and on this account I would condemn them unless one has no other means at hand. The resourceful man will of course get a specimen when important for diagnosis with whatever material is at hand, but this is no excuse for the neglect to use proper facilities when procurable.

We will now consider in detail the apparatus and technique designed to best accomplish these ends.

The Cover Slip. Absolute Cleanliness.—The cover slip should be the thinnest made and square in shape (Bausch and Lomb, No. 1, $\frac{1}{5}$ in. (see Fig. 745, 1). The thicker cover slips are often too thick for the focus of the one-twelfth immersion lens, and not infrequently specimens from important cases at a distance from the laboratory and received by mail cannot be examined accurately owing to this annoying condition. It is a good rule for those engaged in blood work not to have the thicker cover slips under any circumstance.

The Slide.—For the same reason the *thin* slide should be employed (see Fig. 745, 2). Two jars, one containing thick slides for urine work, and thin

Fig. 746.—Method of Making Puncture for Fresh and Dried Specimens of Blood. Shows position of hands and wrist just as puncture is about to be made.

for blood work, will be found a convenient arrangement. These cover slips and slides should be kept in fifty per cent. alcohol and when about to be used should be rubbed with a bit of clean silk, or some fabric free from lint specks. Pocket-handkerchiefs which have been many times ironed are free of loose lint and therefore are very suitable for this. The slide and cover slip should be rubbed quite free of any cloudiness or dust and then dried. This last can be done either by pouring a little ether over the glass and rubbing again or by heating gently over a flame. The cleaned slip and slide should now be laid upon a sheet of clean paper. The following instruments, as first recommended by W. S. Thayer of the Johns Hopkins University, will be found to be the best.

The clamp forceps is so made that the extreme tips of the limbs meet before any other portion, and this enables one to take a small but firm grasp of the cover slip (see Fig. 745, 4, *b*). The clamp, moreover, enables the operator to give his whole attention to following the technique, as given below, without being diverted by keeping a grasp on the cover slips. By placing the cover slip in the clamp forceps it can

Fig. 747.—Method of Taking Drop of Blood for Fresh and Dried Specimens of Blood. Shows how to hold forceps and ear, how to steady hands, and the extent of grasp of cover slip by clamp forceps.

be kept free from dust and moisture from the fingers and will be ready for use.

The lobe of the ear is by far the best locality for puncture, for the following reasons: (1) Less sensitive; (2) the act of puncture and the blood are not seen by the patient, important with nervous people and children; (3) pressure, if necessary, is more readily exerted and produces better results; (4)

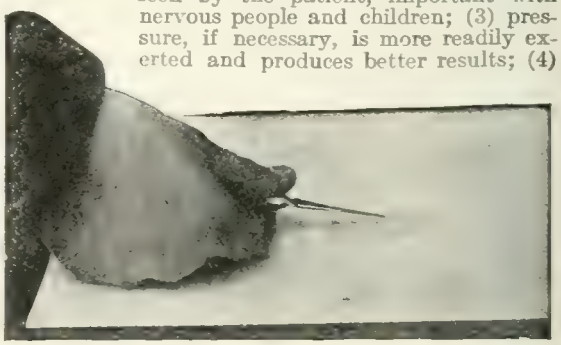


Fig. 748.—Correct Position of Hand in Holding Clamp Forceps. Cover slip resting on slide. The illustration represents the position just before the forceps are opened and jerked away.

the skin in this locality is softer and cleaner; (5) there is less likelihood of subsequent infection.

The lobe of the ear is first gently wiped (not rubbed, as this produces hyperemia) with silk or old linen moistened in alcohol and the skin is then

EXPLANATION OF
PLATE XIII.

EXPLANATION OF PLATE XIII.

(Drawn by Dr. E. Dunning.)

Fig. 1.—Gross appearance of well-taken fresh-blood specimen.
Fig. 6.—Microscopic appearance of well-taken fresh-blood specimen.

See p. 161, *Characteristics of a Good Fresh-Blood Specimen.*

Fig. 3.—Microscopic appearance of poorly taken fresh-blood specimen.
Fig. 5.—Microscopic appearance of poorly taken fresh-blood specimen.

See p. 161, *Characteristics of a Poor Fresh-Blood Specimen.*

Fig. 2.—Microscopic appearance of the Thomas-Zeiss counting stage with normal blood diluted with Toison solution. Red cells unstained; white cells stained blue. This is with the low-power objective (3 Leitz) which takes in all sixteen squares (see Fig. 760, p. 167), but does not magnify the cell as much as the higher power (see Fig. 4), and which therefore greatly increases the task of counting.

See p. 168.

Fig. 4.—Same as Fig. 2, except that the blood is that of leukemia (120,000 leucocytes to the cubic millimeter), and the objective is of high power (7 or 9 Leitz). This takes in only one-sixteenth of the entire field, but it renders the corpuscles much more readily distinguishable.

See p. 168.

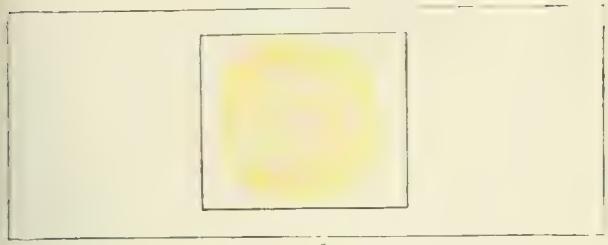


FIG. 1.

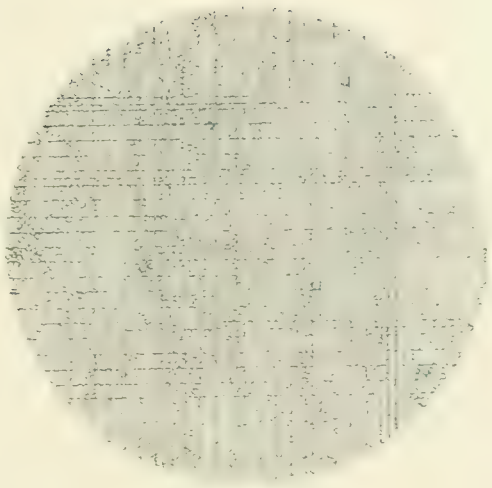


FIG. 2.

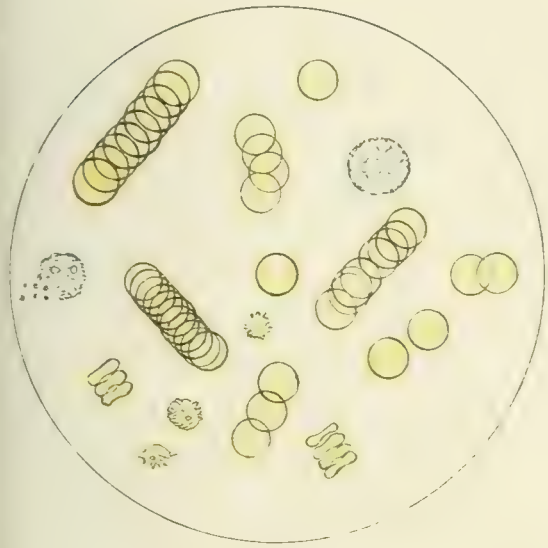


FIG. 3.

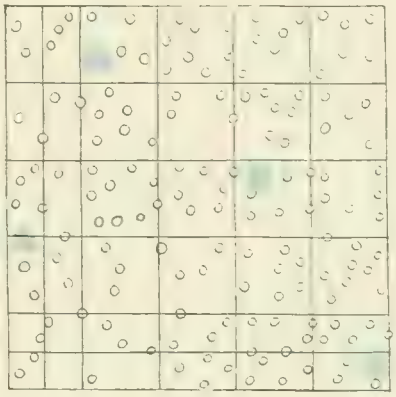


FIG. 4.

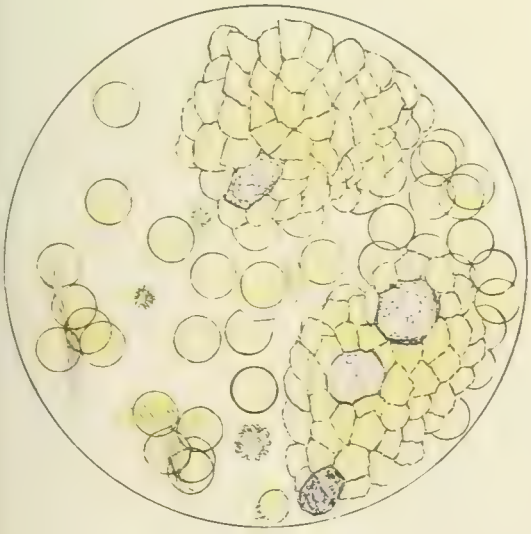


FIG. 5.

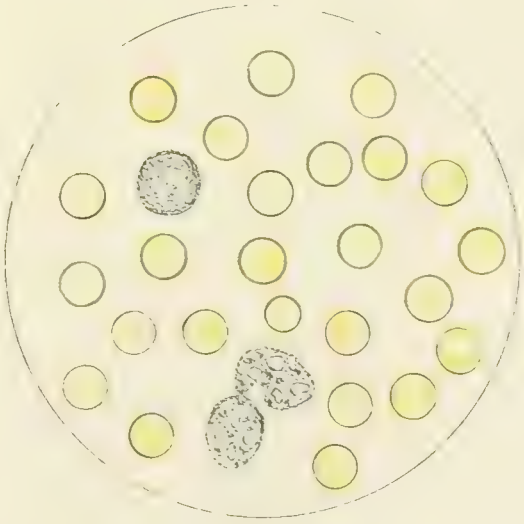


FIG. 6.

HUMAN BLOOD

dried with ether. If ether is not to be had, it is better either to dilute the alcohol three or four times or to use distilled water. Alcohol if left on the skin hardens the blood and so injures the specimen.

The Sticker.—The sticker is now employed (Fig. 745, 3). There are many of these on the market. That recommended by F. C. Wood[1] in his work on Diagnosis is inexpensive and practical. The important requirements are that it shall be extremely sharp and diamond shaped on cross section; the object being to produce a similarly shaped wound, and therefore one which will the more readily bleed. A surgical needle may be used, but an ordinary needle or pin is very unsatisfactory. If, however, one or the other of the latter is all that can be obtained, it should be boiled, flamed, or placed in ninety-five per cent. alcohol. When cleanliness is observed it is only necessary to dip the end of the sticker into alcohol before and after making the puncture.

The most dependent portion of the lobe of the ear is now punctured by a stabbing or staccato motion, the sticker being held as in the illustration (Fig. 746). The common error is to make too deep a wound causing unnecessary and inconvenient bleeding. The first drop is wiped away, the second allowed to flow, if possible without pressure being made upon the skin. If pressure be necessary it should be exerted far away from the point of puncture, so that this artificial means shall not alter the character of the drop taken for examination.

Avoid chilling the blood. It must be remembered that the blood is being submitted to a lower temperature than normal in this proceeding, and in order to *avoid chilling the blood* it is a good plan to warm the slide and cover slip over a spirit lamp, or to have another person briskly rub the slide with a bit of silk or old linen.

The clamp forceps holding the cover slip (see Fig. 745, 4) is now brought toward the ear, and the under surface of the cover slip—and therefore that free from dust—is made to touch the *apex of the drop* of blood, *not the skin of the ear* (Fig. 747). The cover slip is at once carried to the warmed slide and gently lowered.

Avoid rough treatment. The cover slip should not be dropped on the slide. One side of the cover slip should be rested on the slide and gently lowered until the limb of the forceps touches the slide. The forceps is then opened and by a quick jerk drawn away (see Fig. 748). The slide should not be pressed down or moved when once down, as by so doing the corpuscles are distorted or broken.

Avoid exposure to air. It must be remembered also that the air is a destructive medium to the blood, and the time occupied for these steps must be as brief as possible.

The cover settles and the good blood specimen spreads *equally in all directions*, being for the most part circular with fine spicules at the periphery of the circle. The drop should not be so large as to reach the margin of the cover slip when on the slide.

This technique may be summarized as follows:

1. Apparatus. Thin slide, square thin cover slip. sticker, and clamp forceps. Alcohol, ether, spirit lamp, silk cloth or old linen.
2. Absolutely clean point of puncture and apparatus.
3. Seize cover slip in clamp forceps and place near at hand.
4. Light puncture of the most dependent portion of lobe of ear.
5. Warm slide and cover slip gently over spirit lamp; rub slide briskly with silk or old linen.
6. Wipe away drop from point of puncture. (If pressure is required, exert it far away from point of puncture.)
7. Touch apex of second drop with under surface and center of cover slip.
8. Place cover slip promptly but gently on slide; do not touch cover slip after placing it on slide.

Characteristics of a Good Fresh-blood Specimen.—Gross. 1. Blood does not reach margin of cover slip. 2. Is of a circular shape with fine spiculated appearance at periphery. 3. Is thinner in the center than at margin of specimen. (See Plate XIII., Fig. 1.)

Microscopic. 1. Corpuscles each lying separately with some little space between—not in rouleaux. 2. Majority of corpuscles stationary. 3. Each corpuscle circular—*not crenated.* (See Plate XIII., Fig. 6.)

Poikilocytosis is of course pathological and cannot be avoided; crenation is, generally speaking, not pathological, being usually due to faulty technique. (See Plate XIII., Figs. 3 and 5.)

Characteristics of a Poor Fresh-blood Specimen, and such as condemn it for examination.—Gross. 1. Blood thick and oozing out from under cover slip indicates that too much blood has been taken. 2. Irregular shape indicates either that too much blood has been taken, or that dust has been on the slip or slide, or that the blood has been chilled. 3. Thick at one point and partially spread at another indicates dust or moisture. 4. Lump of blood—no spreading—indicates general uncleanliness.

Microscopic. 1. Structureless masses. 2. Abundance of rouleaux. 3. Much crenation. 4. Corpuscles closely placed, giving tiled-floor appearance. 5. Corpuscles floating about specimen. 6. Corpuscles ragged and mutilated. 7. White corpuscles broken into granular collections. (See Plate XIII., Figs. 3 and 5).

2. What Can be Learned from Fresh Specimens of Blood.—The examination of the fresh specimen has of late years been much neglected in favor of the stained specimen. This is unfortunate, especially for beginners, because many features of the blood observed in the fresh specimen are missed and one is apt to form false conceptions of the corpuscle and its biological characteristics from the exclusive study of the dead cell. It is uncalled for here to discuss fully this opinion. In spite of the immense aid which the stains have proven to blood work the writer urges that in all routine examinations the fresh blood be observed first. In hospital work this rule should be insisted upon and the beginner who does not train himself in the thorough study of the fresh specimen first, will place himself at a decided disadvantage in more advanced work on the blood. Perhaps the study of the malarial parasites has suffered more than any other subject in blood work in this neglect of fresh blood examination.

When the precautions laid down in the foregoing have been observed, the following objects can be distinguished:

1. *The Red Blood Corpuscles.*—Erythrocytes—non-nucleated in the normal.

Size.—Normocytes, 7μ. Normal variations. 6 to 9μ in adults, 3 to 10μ in infants. (Note: μ = micron = $\frac{1}{25\frac{1}{400}}$ of an inch. It is well to become familiar with the size of the red cell, and to use it as a unit of measurement when speaking of other bodies, as twice, thrice, etc., the size of the normal red cell.)

Microcytes, cells under 6μ—smallest 2 to 3μ.

Macrocytes, cells measuring 9 to 12μ.

Megalocytes, cells measuring 12 to 16μ.

Gigantocytes, cells measuring over 16μ. These cells of varying size are found in anemia, leukemia, and cholemia. The presence of ten per cent. of such cells is considered diagnostic of pernicious anemia.

Shape.—Biconcave discs normal.

Poikilocytes, Pathological.—Variations in shape. Anisocytes (ἄνισος, unequal, uneven) may be applied to cells varying in size and shape, though some authors use it to signify cells varying in size only. The

wrinkled cell is seen in pernicious and other *grave* anemias.

Physical Properties—Elastic, fragile, normal. It is very probable that in life this property of elasticity and the biconcave shape enable the cell to adapt itself in health and disease to variation in contents. If this impression is correct the cell is capable of great service in maintaining, under the severe strains of circulatory changes, the vital requirements of the tissues.

Schistocytes, fragments of cells. Tend to form rouleaux. Become crenated. May contain bright round spots termed "artifacts."	Conditions usually due to faulty technique and not usually characteristic of the living cell.

The adjective artifactitious, or simply factitious, might be applied to the last three conditions, as they are usually the result of manipulation.

Color—pale yellow. Red only in mass. Even the yellow color is not uniformly distributed. The normal cell appears pale in the center owing to the margin being thicker than the center (biconcave discs).

Lake-like colorless areas (necrobiosis) with irregular shape and margin in the red cells, due to deficiency of hemoglobin, termed by Maragliano "degeneration areas," called also vacuoles, are seen in anemia.

These areas are pathological and must be distinguished from crenation points viewed from above (full face view) and from artifacts in general. The hyaline stage of the malarial parasite resembles these Maragliano areas as well as artifacts. The parasite is less refractile and shows ameboid movements.

Crenation point viewed from above. Artifact spots. Degeneration areas of Maragliano. Hyaline stage of malarial parasite.	To be carefully differentiated.

The colorless or shadow corpuscles, described first by Norris, are seen in the blood of anemia from toxic agents and burns. These are red cells deprived of hemoglobin. They can be artificially produced by adding water to the blood specimen.

The deeply colored (unstained) red cell is seen in pernicious anemia.

The brassy or metallic looking shrunken red cell is seen in estivoautumnal malaria.

2. *The Nucleated Red Corpuscle.*—Nucleated red cells are found in the (human) peripheral blood *normally* in the embryo, in premature infants, and in young infants; *pathologically* in anemia, leukemia, and the pseudoleukemia of infants. It should always be remembered that infants especially and even older children present many ephemeral blood peculiarities which while not associated with any definite symptom-complex cannot be wholly dismissed as insignificant. Whether these are manifestations of normal developmental phenomena or of defensive processes is unknown.

The varieties of nucleated red cells *observable in the fresh specimen.*

Microblast. Normoblast. Macroblast. Gigantoblast.	The relative sizes of these cells correspond to the sizes of the similarly named non-nucleated red cells given above. Thus the microcyte corresponds in size to the microblast, etc.

The nuclei of these cells present many important variations in shape, number and texture, all of which can better be studied in the stained specimen, under which head the nucleus will be described.

3. *The White Blood Corpuscles.*—Nucleated Cells.

Small Mononuclear or Small Lymphocytes.

Large Mononuclear or Large Lymphocytes.

Transitional Mononuclear or Transitional Lymphocytes.

Polynuclear Leucocytes.

Eosinophiles.

Myelocytes in leukemia. (The mast-cells cannot be detected in the fresh specimen.)

An approximate idea of an increase in the white cells as a whole, and one or other variety of these individually, can be had from the fresh specimen. More than four or five white cells, in a *well-spread* field, with a one-twelfth immersion lens may be taken to indicate a leucocytosis. In lymphatic leukemia the increase in the small mononuclear leucocytes is readily appreciated; so also the presence of the cells normally found in the bone marrow, as the myelocytes, can be detected in the fresh specimen in cases of splenomedullary leukemia. In inflammatory leucocytosis the increase in the polynuclear leucocytes can be noted. The increase in the eosinophiles, so important a diagnostic sign in trichinosis, etc., can also be detected.

The size, shape and texture of the nucleus as well as the varieties of granules of the white cells can be better studied in the stained specimen, under which head these will be described.

4. *The Blood Plate and the Plaque**—non-nucleated.

Size—One-seventh the size of the red cell (1 μ).

Shape—irregular.

Color—colorless.

Not visible normally.

One of the most marked characteristics of these corpuscles is their tendency to adhere to one another and to foreign bodies. Occasionally in a well taken specimen a few plates may be seen. They usually, however, disappear rapidly when taken from the circulation and in order to observe them the specimen must be either stained or the following precaution must be taken.

A drop of Hayem's or Pacini's solution† is placed over the point of puncture (the finger must be used for this purpose) and the blood allowed to mingle with this preservative fluid. The cover slip is applied to the drop in the same way as when taking a fresh specimen. With the immersion lens the plates can now be readily seen. There are a number of other preservatives a full discussion of which by J. H. Pratt[2] has been published.

We have no systematic work upon the clinical significance of the presence of these bodies.

The writer has noted them in great numbers (without the use of a preservative fluid) in the blood of certain pneumonia cases, in a case of grave anemia secondary to malaria, and in a case of Hodgkin's disease.

The work of Osler, Bizzozero, Schimmelbusch, Welch, and Eberth has proven that these bodies are separate corpuscular elements of the blood. Their significance and association with disease is yet quite uncertain. Welch's work goes to show that these bodies are the active agents in the formation of the white thrombus; but even this has not, as yet, been of any clinical value.

J. H. Pratt,[3] working in Krehl's clinic, made an especial study of the relation of the plates to coagulation time and of the methods by which the plates could be enumerated. A consideration of the latter will appear in the section on "Blood Corpuscle Counting," below. Pratt's conclusions are that coagulation time is not "determined by the number of plates in

* The term plate is here used to refer to the corpuscles; plaque to the aggregation of these plates. Platelet, a term synonymous with plate, is best discarded.

† *Hayem's Solution.*

Bichloride of mercury..	0.5
Sodium sulphate.....	5.
Sodium chloride.....	1.
Distilled water.....	200.

Pacini's Solution.

Bichloride of mercury...	2.
Sodium chloride.....	4.
Glycerin.....	26.
Distilled water.....	226.

the unit volume of blood" and that coagulation is not "due to the presence of a certain amount of coagulation-producing substance derived from the plates." Pratt's work answers these two important questions and his conclusions (especially those upon plate enumeration) bring the plates into greater clinical importance, but as yet these bodies cannot be said to aid materially in diagnostic considerations.

The relation of blood plates to the pathogenesis of purpura hæmorrhagica has been exhaustively reported upon by W. H. Duke.[3a]

5. *Fibrin* does not, normally, appear for some time in a well-taken fresh specimen. Its presence shortly after taking the specimen is therefore of pathological significance. We have not been able as yet, however, to attach any diagnostic value to this condition.

6. *Blood Dust*, hemoconia (hemokoniosis, literally, blood full of dust, of Müller) can be seen as floating particles about one-twentieth or one-thirtieth the size of the red cell. No satisfactory explanation of the significance of these particles has as yet been given. Many of these particles may be fragments of broken corpuscles (Schistocytes), noted above. They frequently present the active (Brownian) motion common to all bodies suspended in a fluid medium and the common error is in interpreting this as intrinsic or vital motion. The corpuscular elements of the blood equal in bulk about one-half the whole blood mass of the body; the plasma being the other half, the corpuscles have abundance of space to move freely in the liquid medium. It is hardly necessary to say that microorganisms cannot be observed in the fresh specimen, though beginners repeatedly mistake floating particles in the blood for such.

Blood Parasites.—The tertian and quartan malarial parasite in all its stages of development, and many of the stages of the estivoautumnal malarial parasite, may be seen with the one-twelfth oil-immersion lens.

The *Filaria sanguinis hominis* may be seen with the 7 or 9 Leitz lens.

The spirochete of relaping fever may be seen with the 7 or 9 Leitz lens. The trypanosome of early stage of sleeping sickness can be seen with the 7 or 9 Leitz lens.

All this information is to be had by the simple procedure of taking, in the way described, a specimen of blood. All these points will be found grouped in the table at the end of this article.

Having ascertained, then, from the fresh specimen that there is a decrease in the number of red cells, or an increase in the number of white cells, it becomes necessary to determine this decrease and increase definitely, for which purpose additional instruments are required.

II. Blood-corpuscle Counting.

1. Evolution of the Modern Counting Apparatus.—It is only of late years that the methods of enumerating the blood corpuscles have been simplified so as to be clinically applicable, the complicated apparatus heretofore used having had place in works on physiology only. It is therefore of value to trace the development of our present simple apparatus from its complicated beginnings. When we look over all the methods employed to accomplish this last, we find that investigators have endeavored to construct apparatus along three separate lines, as follows: 1. Actual enumeration. 2. Centrifugalizing and estimating cells according to amount of sediment. 3. Color changes and opacity due to decrease in number of cells.

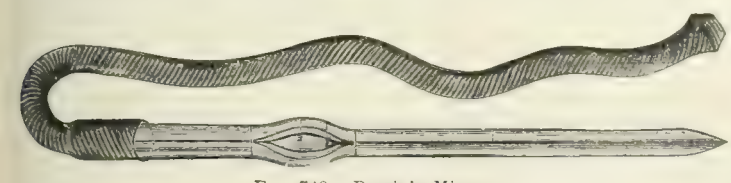


Fig. 749.—Potain's Mixer.

This will therefore be, not a history of blood counting in chronological order, but rather the record of the development of apparatus along these three lines.

1. Actual Enumeration of Blood Corpuscles.—Vierordt was among the first actually to enumerate the red blood cells; and though his apparatus was most crude and his method most complicated, yet his results have been abundantly confirmed by subsequent observers working with varied styles of apparatus. Vierordt's figures were, 5,174,000 red blood cells per cubic millimeter.

Vierordt diluted with a fixed quantity of salt solution a cubic millimeter of blood and then spread this upon a slide. By means of a micrometer he counted every corpuscle. For one enumeration it took an entire week. The result of this work was to establish the following:

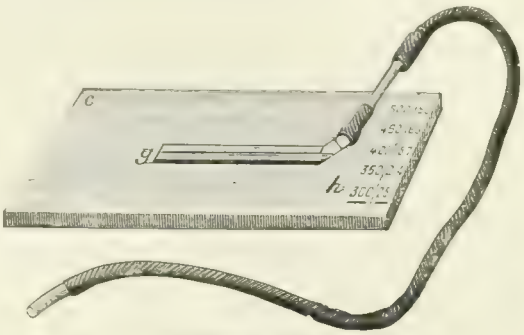


Fig. 750.—Malassez' Artificial Capillary.

(1) A known quantity of blood must be taken, that quantity being the amount contained in a cubic millimeter. (2) A known dilution must be used. (3) A cubic millimeter of normal blood contains 5,174,000 red cells.

At this time, Kölliker, after declaring that "owing to the difficulty of the subject" the most careful estimates can "only be described as approximate," adds: "One method only can be successful, consisting in the direct enumeration of the globules in accurately determined quantities of blood." Welker adds the next improvements (1) in using a stage micrometer, and (2) in counting the corpuscles in a fraction of a large dilution and multiplying the result of this count by the figures required to make the whole cubic millimeter.

Potain's mélangeur or mixer afforded the first means of accurately diluting the blood. This was nothing else in principle, but of cruder make, than the mixer now employed in the Thoma and Zeiss blood-counting apparatus. Fig. 749 shows this mixer.

Potain's mixer was divided precisely as is the Thoma-Zeiss mixer, into a dilated and a capillary portion, the capillary portion being exactly $\frac{1}{100}$ part of the whole. The dilated portion of the Potain mixer contained the little glass ball, as in the Thoma-Zeiss apparatus. Malassez combined this suction capillary pipette with an artificial capillary in the following manner: Blood is drawn up by suction into the Potain mixer to the 1 mark, and a diluting fluid, called the "artificial serum" (consisting of gum arabic specific gravity 1.020, one volume; sodium sulphate and sodium chloride, equal parts and each of specific gravity 1.020, two volumes), to the 100 mark, making dilution of 1 in 100. The

pointed end of the mixer is then fastened to a rubber tubing connected with the artificial capillary, as seen in Fig. 750.

The artificial capillary is set in a plate of glass which is divided into fractions of a cubic millimeter, as seen in the illustration. The microscope is adjusted so as to magnify the corpuscles as they lie in the artificial capillary (see Fig. 751), and their number is ascertained for a fractional part of this capillary as marked on the glass plate. According to the fraction of a cubic

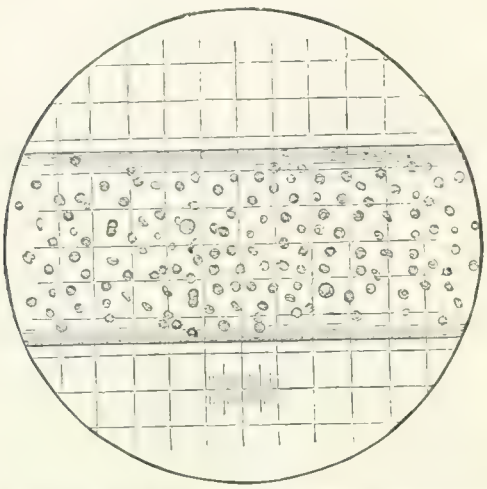


Fig. 751.—Artificial Capillary as it Appears Under the Microscope. × 180 diameters. (From Ranvier.)

millimeter which that portion selected to count represents, the number counted is multiplied.

Suppose one counts the corpuscles in $\frac{1}{100}$ of a cubic millimeter; then 400 times that number multiplied by the amount of dilution represents the number of corpuscles in a cubic millimeter.

This method offered many difficulties: 1. Complicated artificial serum for dilution. 2. Introduction of blood without air into artificial tube difficult. 3. Difficult to clean apparatus.

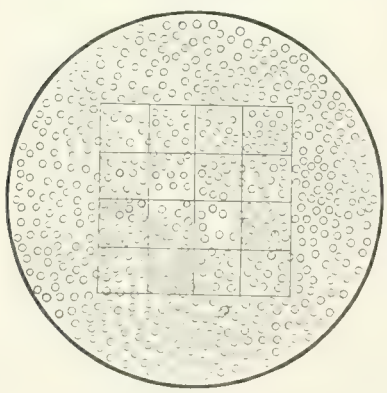


Fig. 752.—Appearance of Corpuscles with Hayem and Nachet's Instrument.

Hayem and Nachet devised an instrument (hématimètre) by which the blood and serum are obtained in two separate pipettes and then mixed in a glass receiver. A drop of this mixture is then placed upon a glass slide arranged as follows: A circular well, similar to that employed in the Thoma and Zeiss apparatus, is constructed with the accurate measurement of one centimeter in diameter and 0.2 millimeter in depth. An eyepiece micrometer ruled in a large square which is subdivided into sixteen squares is then attached. One side of the large square measures exactly $\frac{1}{5}$ millimeter* (see Fig. 752).

* One-fifth millimeter depth by one-fifth millimeter on two sides of square makes the block of blood one-fifth (0.2) cubic millimeter —5×5×5=125.

By counting the cells in the square and multiplying this count by the fraction of a cubic millimeter which this square represents, and the number of volumes of the diluting fluid, the number of cells in a cubic millimeter is ascertained. This is complicated, but, as will be seen later, it has contributed certain points toward the simple apparatus used to-day.

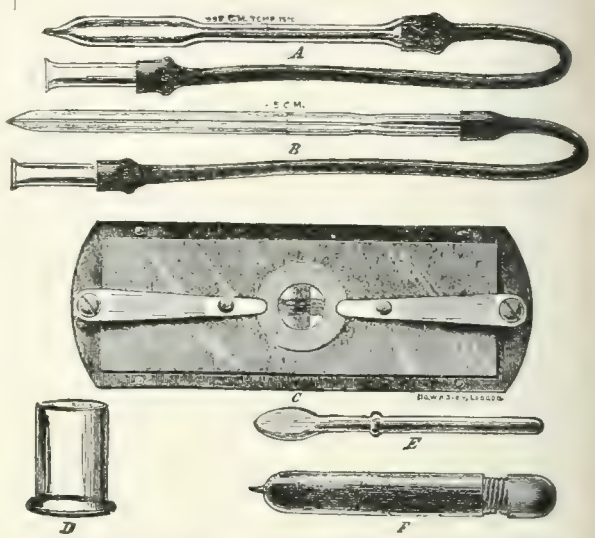


Fig. 753.—Gowers' Hemacytometer (From Kirkes' "Handbook of Physiology," twelfth edition.)

Gowers[4] has described an instrument called the hemacytometer, which more nearly approaches perfection than any already described; it therefore marks what may be considered the border line between the ancient and modern history of blood-counting by the actual enumeration method. Gowers' instrument (see Fig. 753) consists of: A, Small pipette (with rubber mouthpiece for suction) which, when filled (with diluting fluid) to the mark on its stem, contains exactly 995 cubic millimeters. B, Another pipette marked to hold 5 cubic millimeters (of blood). D, Glass jar for mixing (blood and diluting fluid). E, Stirrer (to stir blood and diluting fluid in glass jar). C, Brass plate with a cell one-fifth (0.2) millimeter in depth and with the floor divided into one-tenth (0.1) millimeter squares and a cover-glass held in place by springs.

A standard saline solution of sodium sulphate of specific gravity 1.025 is employed; 995 cubic millimeters of solution are mixed with 5 cubic millimeters of blood with the pipettes. These are mixed in the glass jar. A drop is placed in the cell in the brass plate and the cover slip held down by the springs. The cells are then counted in ten squares, and the calculation for 1 cubic millimeter of which this is a fraction made.

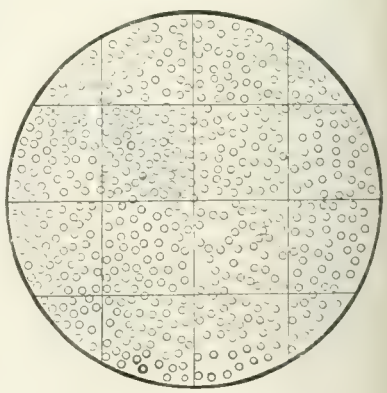


Fig. 754.—Appearance of Corpuscles Under Microscope with Gowers' Instrument.

As we review these descriptions of apparatus we

see that the effort of the inventors has been to overcome certain obstacles, viz., (1) Reduction of the corpuscles to a countable number. Vierordt accomplished this by dilution and by fixing the area to be counted to the cubic millimeter. (2) Obtaining the blood so as to prevent clot, and to dilute accurately. Welker showed the value of accurate dilution. Potain's mélangeur best accomplished this. (3) Spreading the blood upon such an area and of such a depth as to enable the observer to see each corpuscle separately. Malassez accomplished this with a long narrow tube; Hayem and Nachet with a cell whose depth was a fraction of a cubic centimeter. (4) Mapping out the area so that the eye could navigate upon it. Hayem and Nachet accomplished this with an eye-piece micrometer. Gowers, without an eye-piece micrometer, but with a marked-out slide.

All these methods depend (as Kölliker has pointed out) upon the following principles: (1) A known quantity of blood for estimation (one cubic millimeter); (2) a known dilution of a known quantity of blood; (3) a known fraction of a cubic millimeter to be counted.

2. Apparatus and Technique employed in Corpuscle Counting.—Upon these principles and with the information obtained from the foregoing inventors, Thoma amd Zeiss have constructed their apparatus. This combines the mélangeur of Potain and the mapped-out cell of Gowers.

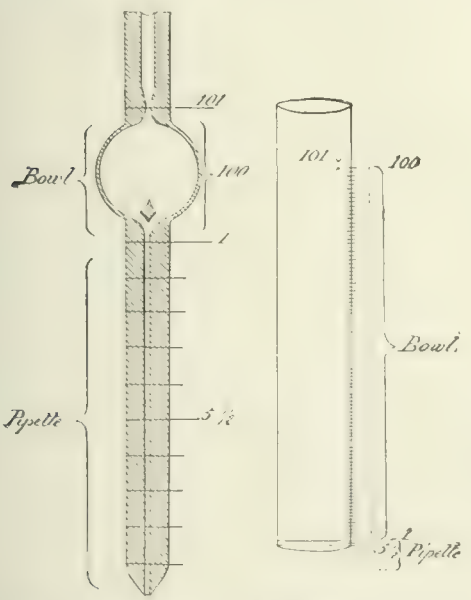


Fig. 755.—The Mixer of Thoma and Zeiss Corpuscle-Counting Apparatus. Shows principle of dilution by comparison of pipette (a necessary instrument in dealing with a coagulable fluid like blood) with an ordinary receiver (in which a non-coagulable fluid could be diluted).

Principle of the Thoma-Zeiss Mixer.—The mixer consists of a capillary portion and a dilated or bulb-like portion. The capillary portion enables one to procure a fixed quantity of blood that is free from clotting, if promptly taken; and the bulb portion enables one to procure a fixed dilution. The principle of this mixer is best understood by reference to the diagram shown herewith (Fig. 755).

Suppose the fluid to be diluted were wine or some non-coagulable fluid. Then we should pour the wine into the receiver, as shown in the diagram, up to the mark 1, and the diluting fluid up to the mark 100. This would be 1 to 100. Were we to pour the wine up to the .5 mark only (or ½ of 1), and the diluting fluid up to 100, we should have half as much wine as before to the same amount of diluting fluid, or in the proportion of 1 to 200. Half the fluid to be diluted with the same amount of diluting fluid has the same result as doubling the amount of the latter.

Now blood cannot be poured in this way. An instrument must therefore be devised by which the blood can be taken free from clotting. Our receiver, therefore, is converted into a capillary tube and our pouring is replaced by suction. That portion of the receiver marked off as 1 is converted into the pipette, and that portion of the receiver marked off as 100 is converted into the bulb. We now have an instrument by which a definite quantity of blood can be drawn up together with a definite quantity of diluting fluid. This instrument, when full, represents 101 of blood and diluting fluid, or 1 of blood to 100 of diluting fluid. If the blood be drawn to the .5 or ½ mark and the diluting fluid to the 100 mark we have 1 to 200.

The Thoma and Zeiss apparatus is occasionally provided with two mixers similar in all respects except that one is larger than the other; one for counting the white cells, the larger one; and one for counting the red cells, the smaller one. That for counting the red cells is all that is necessary, and, as will be seen later, is preferable to two separate proceedings.

The diluting fluids, at first so complicated, have been much simplified. The object has been to obtain a medium as nearly as possible like that in which the corpuscles normally float.

Diluting Fluids: (1) Normal, better named physiological, salt solution.* (2) Acetic acid 1 in 300 destroys the red cells and accentuates the nuclei of the white, and is therefore valuable in counting the white cells alone. (3) By using a basic stain together with the preservative salts the results obtained separately by the other fluids are combined. The most satisfactory of these is the Toison solution.

Formula.

Sodium chloride	1.000 gm
Sodium sulphate	8.000 gm.
Glycerin	30.000 c.c.
Water	160.000 c.c.
Methyl violet	0.025 gm

In the preparation of this solution it is advisable first to mix the sodium chloride and sodium sulphate thoroughly, and then to add these to the glycerin and water—the methyl violet being added last. The brackets in the above formula show these steps in the preparation.

This solution must be kept in the dark and must be filtered from time to time as it loses its color and develops a fungus growth which seriously plugs the pipette, and appears in the specimen as débris. No count made when such detritus is present is reliable. The solution preserves the red cells and by means of the methyl violet stains the white cells a light purple, making the latter readily distinguishable and enabling one to make the count of both red and white cells in one process.

Principle of the Counting Well.—Having thus an apparatus for taking a fixed quantity of blood with a fixed quantity of diluting fluid, we must next have a means of counting the corpuscles. For this a glass slide is constructed, with a well in the center of known dimensions. It must be remembered that each of the various parts of this apparatus described has been constructed to overcome an obstacle. By diluting the drop in a mixer the clotting was overcome and the number of corpuscles reduced to a countable figure.

* Normal in chemistry indicates a solution containing the sum of the atomic weight of the salt employed in grams to 1,000 c.c. of distilled water. As this is not the case with so-called normal salt solution, the term is misapplied. Physiological salt solution is, roughly, NaCl 3j. to the Oj. distilled water.

The well which we are about to describe (1) reduces the cubic millimeter to a depth through which it is possible to see each corpuscle separately (a cubic millimeter of blood and fluid to the dilution of 200 times would be so thick and contain so many corpuscles that the task would be beyond human skill); (2) maps out that area so that the eye can find, as it were, the longitude and latitude of any point in the sea of corpuscles.

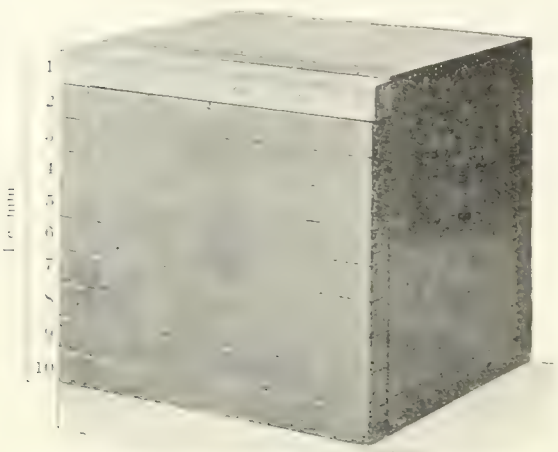


FIG. 756.—A Cube Representative of the Amount of Blood from Which Corpuscle Enumeration is Made. The block represents 1 c.mm.

To what fraction of a cubic millimeter is it necessary to reduce this (cubic millimeter of) known dilution of blood in order to make it possible to see and count each corpuscle? This fraction is found to be one-tenth of a cubic millimeter in 1 to 100 or 1 to 200 dilution of blood.

The illustration (Fig. 756) represents a millimeter cube. If this consisted of blood, the depth would be too great for the human eye to penetrate and would contain so many corpuscles as to be beyond human

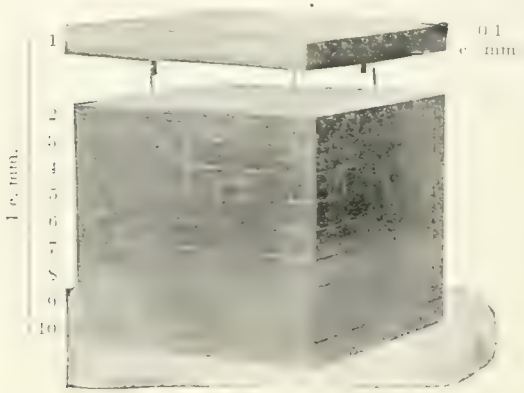


FIG. 757

skill to enumerate. We therefore retain two dimensions of the cube, but take only one-tenth of the depth. This layer of blood is therefore one-tenth of a cubic millimeter in a 1 to 100 or 1 to 200 dilution (see Fig. 757).

The counting stage, to fulfil these requirements, must be constructed as follows: The bottom of the well upon which the corpuscles rest must be laid off with a square whose dimensions are one millimeter each way, and the well must be one-tenth of a millimeter in depth. The illustration (Fig. 758) shows the full face view of the counting stage. In the center is seen the bottom of the well with a square laid off measuring one millimeter each way.

The second illustration (Fig. 759) shows the profile of this stage with the cover slip in place. The measurement from the under surface of the cover slip to the bottom of the well is exactly 0.1 millimeter.

When, therefore, a drop of the diluted blood is placed in this well and the cover slip is in place, those corpuscles which we see contained within the square, the dimensions of which are 1 millimeter each way and 0.1 millimeter in depth, are the contents of a cube of diluted blood measuring $\frac{1}{100}$ of a cubic millimeter.*

Principle of the Ruling of the Counting Well.—We now turn to the marking out of a millimeter square which is to render it navigable. Here, as before, an obstacle is to be overcome, viz., the inability of the human eye to keep its bearings when viewing several thousands of corpuscles.

The first subdivision of this area (as first done by Nachet and Hayem on the eye-piece and by Gowers on the stage) is into sixteen squares. But even this does not overcome the difficulty, and it is necessary still further to subdivide each one of these into twenty-five squares (Fig. 760). It now becomes necessary to establish some boundary mark for these sixteen large squares, each consisting of twenty-five small squares. This is done by bounding each of the

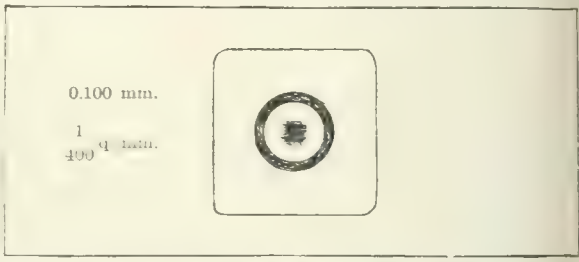


FIG. 758.—Full-Face View of Counting Stage. (Drawn by Dr. E. Dunning.) [0.100 mm. = depth = $\frac{1}{10}$ of a millimeter; $\frac{1}{400}$ q.mm. (German quadrat, square) = smallest square which measures $\frac{1}{400}$ of a square millimeter ($25 \times 16 = 400$).]

sixteen squares on two sides with double lines. Now we can readily count the corpuscles in one of the large squares which is bounded on two sides by the double lines, and realize that this represents one sixteenth of the field; or in one of the small squares, and realize that this represents $\frac{1}{25}$ of $\frac{1}{16}$, or ($16 \times 25 = 400$), $\frac{1}{400}$ of the whole millimeter square. On the glass slide (Fig. 758) will be noticed the figures 0.100

* These microscopic dimensions, but for the present simple method of construction, would render this instrument in the making a very costly and delicate affair. In the manufacture of this counting well a glass slide similar in length and breadth, but a little thicker than that employed for general microscopic work, is used. Upon a round block of glass the millimeter square is cut or pressed. This block of glass is cemented to the center of the glass slide and forms the bottom of the counting well. Another piece of glass, like a thick cover-glass but with *a round hole* cut in the center, is cemented upon the slide, so that the block of glass already in place occupies, but does not exactly fit, the hole. The difference in measurement, from above down, between the upper surface of the round block of glass and the upper surface of the glass with the hole through it is just 0.1 millimeter. Thus the well with a millimeter square marked at the bottom and 0.1 millimeter in depth is formed. The fact that the block of glass does not completely fill the hole in the outer piece of glass explains why there is left about it a groove into which the blood flows, if more than is required exactly to cover the block of glass is blown into the well. This seems an objection, as currents are thus produced allowing many corpuscles to flow out of the mapped area. There seems no good reason for the presence of this groove except possibly that it obviates the additional expense of making the block of glass exactly fit the hole.

millimeter, referring to the depth, which is one-tenth of a millimeter; also $\frac{1}{400}$ square millimeter, referring to the smallest squares, each one of which measures $\frac{1}{400}$ square millimeter ($\frac{1}{20}$ of $\frac{1}{20}$ = 400). (Fig. 760.)

Once these mathematical facts are clearly understood, one may count in many different ways. One small square may be counted, and the result multiplied by 400; or 25 small squares, and the result multiplied by 16. The best method, however, will be given in the following description of the use of the apparatus.

Now that we understand the principle of the apparatus, let us proceed to its use:

Fig. 759.—Profile View of Counting Stage. (Drawn by Dr. E. Dunning.)

In order to obtain the blood the ear is punctured as for a fresh specimen, and the tip of the capillary tube *inserted into* the drop and retained there while *gentle* suction is exerted, and the blood drawn either to the 1 mark, or the .5 or ½ mark, as shown in Fig. 761. The latter is preferable, for the following reasons: (1) Less blood. (2) Difficult to stop sharply at the 1 mark without the blood passing on into the bowl and necessitating cleaning the instrument and beginning again. In using the .5 mark, if the blood pass the mark it may be soaked off the tip of the pipette with linen or blotting paper until the column stands opposite the .5 mark—cleaning, etc., not being necessary.

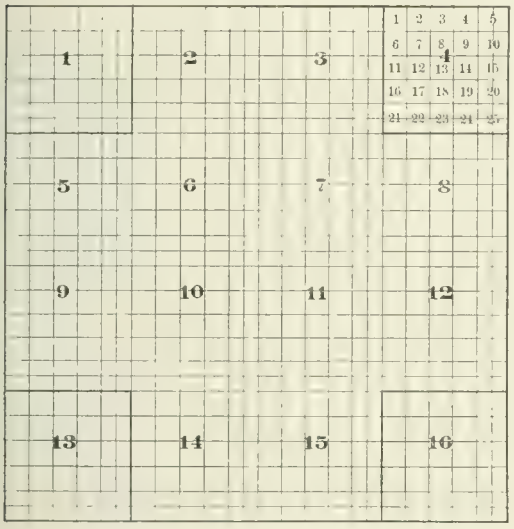


Fig. 760.—Subdivisions of Counting Field of Thoma and Zeiss Apparatus. (1 sq.mm. = $\frac{1}{25}$ sq.mm. = $\frac{1}{400}$ (25 × 16) sq.mm.)

As promptly as possible, to avoid clotting, the pipette is *submerged* into the diluting fluid; and then, but not till then, suction is again made until the fluid stands opposite the 101 mark (Fig. 762). Suction must be gentle throughout, and especially so as the fluid is approaching the 101 mark, as it readily pops into the rubber tubing. The tip of the pipette must *always be immersed* in the fluid being sucked up, whether it be blood or diluting fluid, otherwise air enters the pipette and destroys the specimen.

Directly the diluting fluid has reached the 100 mark the finger is placed on the tip of the pipette and the whole shaken in order that the corpuscles may, by the aid of the small glass ball in the bulb portion of the mixer, be thoroughly mixed with the diluting fluid (Fig. 763). As the pipette contains the diluting fluid and no corpuscles, this must be emptied; and to

Fig. 761.—Shows Method of Drawing Blood into Mixer. Diluting fluid near *at hand*.

be certain that this is done the bulb of the mixer is emptied one-third by blowing the fluid out. The diluting fluid should be allowed to act upon the blood in the mixer for five or ten minutes before the drop for counting is taken from the mixer.

If the blood is not to be counted at once or to be carried to the laboratory some distance away, a thick rubber band should be placed over the openings of the mixer, otherwise the blood will leak out and destroy the accuracy of the specimen. The tip of the capillary end of the mixer is very sharp and will at times pierce the rubber band and allow the blood to leak. Two bands one on top of the other or one not too tight will obviate this.

The counting stage is now employed. This stage and the cover slip must be free from dust particles. The latter (the cover slip), grasped

Fig. 762.—Thoma and Zeiss Corpuscle-Counting Apparatus. Drawing diluting fluid into mixer. The blood has already been drawn in.

with the clamp forceps, is placed conveniently at hand. A thick cover slip with accurately level surfaces, to prevent bending, is provided with the apparatus; but as this interferes with the use of the high-power lens, it is an objection. An ordinary cover slip may be used, if care is taken not to press down upon it with the objective. From the mixer a drop is blown on to the central raised table of the

Fig. 763.—Position of Hands in Shaking Mixer.

counting well (Fig. 764). The drop should not (1) flow into the well, (2) or contain air bubbles, or (3) particles of dirt. The cover slip is lowered *until the fluid touches it*, then the forceps is opened and withdrawn with a jerk as in laying the cover slips for fresh specimen (see Fig. 748). Air bubbles may be avoided by observing the foregoing precautions.

By holding the slide up to the light *on a level with the eye* and making pressure with the point of the forceps upon the cover slip, a series of varicolored concentric rings will be seen about the point of the forceps where it touches the glass. These are the Newton's rings, which are seen only when two pieces of glass are in perfect apposition, *i.e.* when there are no dust particles, etc., between them. The presence of these rings is therefore an evidence that the glasses are per-

Fig. 764.—Blowing Drop from Mixer on to Stage.

fectly clean. Two to three minutes are now allowed for the corpuscles to sink through the depth of one-tenth of a millimeter and rest on the mapped-out bottom of the well. By at once observing the slide under the microscope this sinking process may be seen. We are now ready to count; the lowest-power lens of the Leitz or Zeiss microscope may be used. This takes in its field of vision the whole counting area, but magnifies the corpuscles so slightly that the strain upon the eye is great (see Plate XIII., Fig. 2). The 7 or 9 objective of the Leitz takes in only $\frac{1}{16}$ of the counting area, but does not strain the eye, and is therefore preferable, as with little practice the stage may be gradually moved until the whole area has been examined (see Plate XIII., Fig. 4). As the proportion of white corpuscles to red is about 1 to 700, there will be in a given area much fewer white corpuscles than red; and in the one-tenth of a cubic millimeter there will be about 3 white cells to about 2,100 red cells. The task, therefore, of picking out three white cells in an entire field will be a simple one; while it is more practicable to count only a fraction of the field containing 2,100 red cells, and then compute the total by multiplying the number counted by the fraction adopted (see Plate XIII., Figs. 2–4). The following are the steps to be taken in counting the red and the white cells:

3. Enumeration of the White Blood Corpuscles.—(1) Count cells contained in entire field, *i.e.* 16 squares = $\frac{1}{10}$ of a cubic millimeter; (2) multiply by 10 to make the 1 cubic millimeter; (3) multiply by 100 or 200, according as the dilution has been made.

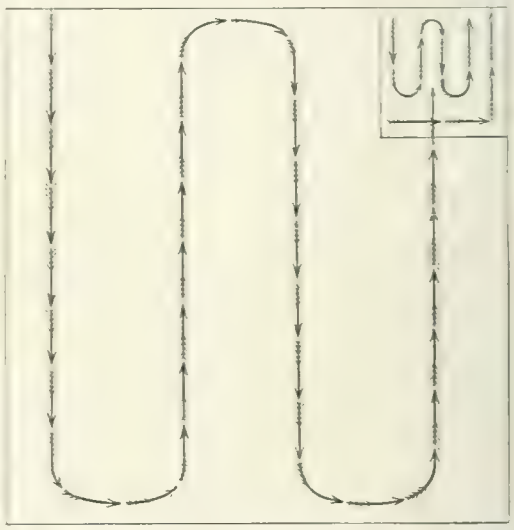


Fig. 765.—The Arrows Indicate the Routes to be taken in Counting the Entire Field and One-sixteenth of the Entire Field.

4. Enumeration of the Red Blood Corpuscles.—(1) Count 4 squares, each consisting of 25 of the smaller squares: 4 squares out of $16 = \frac{4}{16}$ or $\frac{1}{4}$ of the whole $\frac{1}{10}$ of a cubic millimeter; (2) this number multiplied by 4 gives the number contained in the $\frac{1}{10}$ of a cubic millimeter; (3) multiply by 10 and by 100 or 200 as before.

Now it must be remembered that every time we count a fresh drop from the mixer we decrease the range of error; so (*remembering to shake the mixer well each time, as the corpuscles settle rapidly in the bulb*) suppose in counting the *white cells* we take from the mixer 5 separate drops and count each upon the counting stage. An average of the result, obtained by dividing by 5, gives us the number of white cells contained in $\frac{1}{10}$ of a cubic millimeter. This average multiplied by 10 and 100 or 200, as before, will be a more accurate figure than that arrived at by counting one drop only.

Suppose in estimating the red cells we take from the mixer and count two separate drops, counting in the first drop the four corner squares (Squares Nos. 1, 4, 13, and 16 in Fig. 760), *i.e.* $\frac{4}{16}$ of the whole field;

then in *the second drop* the same four corner squares, *i.e.* $\frac{4}{1/6}$ also—our two counts combined will represent $\frac{8}{1/6}$ or $\frac{1}{2}$ of the field; this multiplied by 2 represents the whole field, *i.e.* $\frac{1}{1/6}$ of a cubic millimeter. This multiplied by 10 and by 100 or 200, according to dilution, gives the number of red cells in a cubic millimeter of undiluted blood. These calculations may be expressed as follows:

$$\textit{White Cells:}\ \frac{a+b+c+d+e}{5}\times 10\times(100 \text{ or } 200)=x;$$

a, b, c, d, and e being the counts of separate drops taken from mixer; 5 the average number; 10 for the $\frac{1}{1/6}$ of a cubic millimeter; 100 or 200, amount of dilution; x the number of corpuscles in cubic millimeters of undiluted blood.

$$\textit{Red Cells:}\ \left(\underbrace{(a+b+c+d)}_{(\frac{1}{4}\text{ of field})}+\underbrace{(a+b+c+d)}_{(\frac{1}{4}\text{ of field})=\frac{1}{2}\text{ of field}}\times 2\right)\times 10\times(100 \text{ or } 200)=x;$$

a, b, c, d, each the number of corpuscles in $\frac{1}{1/6}$ of field, therefore together equal $\frac{4}{1/6}$ or $\frac{1}{4}$ of field; plus second count obtained from another drop from mixer equals $\frac{1}{2}$ of field; and multiplied by 2 equals whole field.

One-sixteenth of the field can be readily counted by counting *inside* the double lines up and down, as in mowing a field, and then counting along two sides *in* the double lines. The route for counting in this way is shown by the arrows *in the upper right-hand corner* of Fig. 765. For counting the entire field the arrows in the whole field of Fig. 765 mark the route. This method will be found to save much time.

In order to avoid recounting corpuscles on the line, and to decide to which square these corpuscles belong, the following rule will be found valuable. Count only those corpuscles on the left line of the column down which you are counting, and in the $\frac{1}{1/6}$ square count only those corpuscles which lie on the double-line boundary of the square.

Fig. 766.—Cleaning Mixer. Rubber tube on pipette end of mixer.

With practice a blood count can be made in from fifteen to twenty minutes, unless the blood be from a case of marked leucocytosis or grave anemia in which one wishes an extremely accurate count.

Cleaning the Apparatus.—The Thoma and Zeiss apparatus has received much condemnation from the difficulty experienced in cleaning it. By *strictly* observing the following rules, this difficulty will be almost wholly overcome.

(1) If by accident the blood is drawn into the bulb before being mixed with the diluting fluid, immediately draw up distilled water and proceed to clean as given below. *Do not use alcohol until all trace of blood has been removed.*

(2) Do not draw the blood into the pipette until the bottle holding the diluting fluid *is at hand* and the *cork out of the bottle* (see Fig. 761).

(3) See that the diluting fluid contains no flakes or fungus growth; if these be present, filter the fluid before using.

(4) Dry the mixer by drawing up ether and blowing it out.

(5) See that the rubber tube is free from saliva and foreign material from the mouth. It is well to do this from time to time, while using the apparatus, by detaching the tube from the mixer and blowing it out and then passing distilled water through it. Suppose these precautions to have been taken and the diluted specimen to be in the bulb and our count completed; we then proceed to clean the mixer.

(6) Remove the rubber tube, blow out the saliva, etc., which may have collected (see (5), above). Attach the tube *to the pipette end* of the mixer and blow out the contents of the bulb (Fig. 766).

(7) Replace the rubber tube on the large end of the mixer and draw distilled water into the bulb. Shake the mixer well and blow this water out by reversing the tube as recommended in (6), each time blowing the rubber tube free of saliva.

(8) With the tube on the big end of the mixer draw up ninety-five per cent. alcohol. With tube on pipette end blow this out. This removes the stain. If the glass is not entirely freed from stain, repeat until desired result is obtained.

(9) With the tube on the big end of mixer draw in ether, and then (*without* reversing tube) blow the ether out through the pipette. This shows that the whole apparatus is clear and ready for use next time.

If epithelium or mucus from the mouth, etc., gets into the bulb, it is best removed by drawing undiluted hydrochloric acid up and then introducing an especial make of wire which the writer has suggested to Messrs. Eimer & Amend to procure. It is known in commerce as "stiff brass wire, B. & S. (Brown & Sharp), No. 31 gauge," and has the advantage of being very fine but very stiff, and can be run *the whole length* of the Thoma and Zeiss mixer. With this wire, and *most decidedly with all other wires*, one must be careful to have no kinks, as these may break, leaving the wire in the mixer—an awkward accident.

R. Friedländer of Wiesbaden[5] has described an instrument, devised by himself, for counting leucocytes. He was led to the construction of this instrument by a sense of inaccuracy while using the Thoma and Zeiss counter. His objections to the latter instrument were, first, too considerable a dilution and therefore too few white cells from which to estimate; second, the calculations necessary with the Thoma and Zeiss instrument are so extensive that a small variation in the number upon which these calculations are based means an error of many thousands. Freidländer confirmed these objections by obtaining different results in a number of counts of blood taken from the same individual on a single occasion. In order to overcome these objections Friedländer had Zeiss construct the following apparatus:

A pipette similar to that employed in the Thoma and Zeiss apparatus—dilution 1 in 10 or 1 in 20; a counting chamber 0.222 millimeter deep × 0.3 millimeter square, with the floor divided into squares —16×16=256 squares in all. The double ruling is omitted; a mechanical stage is employed.

In order, by this method, to arrive at a figure expressive of the number of leucocytes in a cubic millimeter, the following formula is employed:

$$\frac{A\times Z}{M\times Q}$$

A = amount of dilution.
Z = number of leucocytes found in these sections.
M = number of sections observed.
Q = the cubic area between the floor of the counting stage and the cover slip—*i.e.* $0.09\times 0.22=0.0198$.

Example: Suppose 192 squares to have been counted and 1,522 leucocytes found; dilution 1 to 20.

$$\frac{20\times 1{,}522}{192\times 0.0198}=8{,}007 \text{ leucocytes in 1 c.mm.}$$

(NOTE: There is a mistake in Friedländer's formula; 1,0198 should be read as above, 0.0198.)

As diluting fluid he employs one-per-cent. salt solution tinged with gentian violet to which is added one-third-per-cent. acetic acid. Thus the red cells are destroyed by the acetic acid and the nuclei of the white cells intensified, and at the same time the cell is stained by the gentian violet.

The writer has had no experience with this instrument. If the steps as laid down in describing the Thoma and Zeiss instrument are followed the results should be as accurate.

As a clinical instrument Friedländer's would seem to be objectionable if for accuracy it is necessary to count a thousand or more cells. Unless we can arrive at accurate results by simple methods an apparatus loses its *clinical* value.

A number of counting chambers have been devised. These differ chiefly in respect of the size of their rulings; the larger ones being given the preference in order to minimize the possibility of error. The following are some of these: counting chamber of Zappert, counting chamber of Gabritschewsky, counting chamber of Miessen.

Corpuscle Enumeration by Means of the Centrifuge.—We now approach the task of corpuscle enumeration from a different point of view. As the corpuscles are particles floating in a fluid, we should be able to precipitate these and measure the precipitate. If, as is the case in anemia, the corpuscles are few, our sediment should be less than in the normal. The task, then, is to throw these corpuscles down. This is done by the use of the centrifuge. This machine was employed at first to obtain serum, and its use for the latter purpose suggested its application as a corpuscle enumerator.

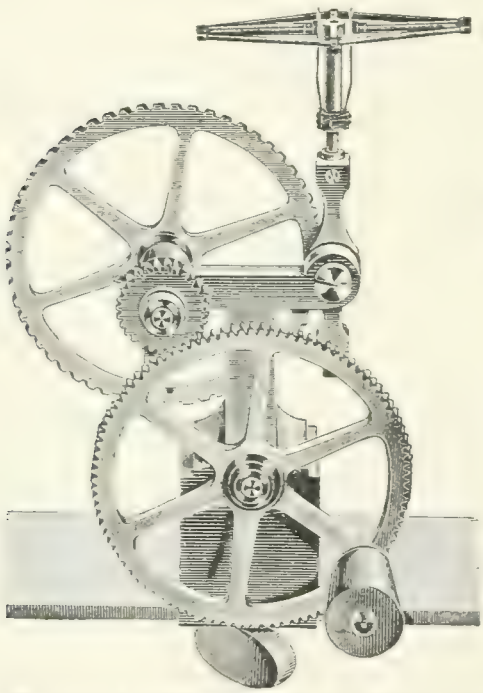


FIG. 767.—Hedin's Hematocrit. (From von Jaksch's "Clinical Diagnosis.")

Principle.—When blood is placed in the tube of a centrifuge and the apparatus rotated, the corpuscles collect as a red mass at the distal end of the tube and the serum as a colorless, semitransparent liquid at the proximal end.

By taking a fixed quantity of blood and subjecting it to a fixed number of revolutions for a fixed time, and by noting and marking the height of the column of corpuscles in the tube filled with blood from healthy individuals, a normal standard is determined. Deviations from this standard may be taken to indicate an increase or a decrease in the number of red cells.

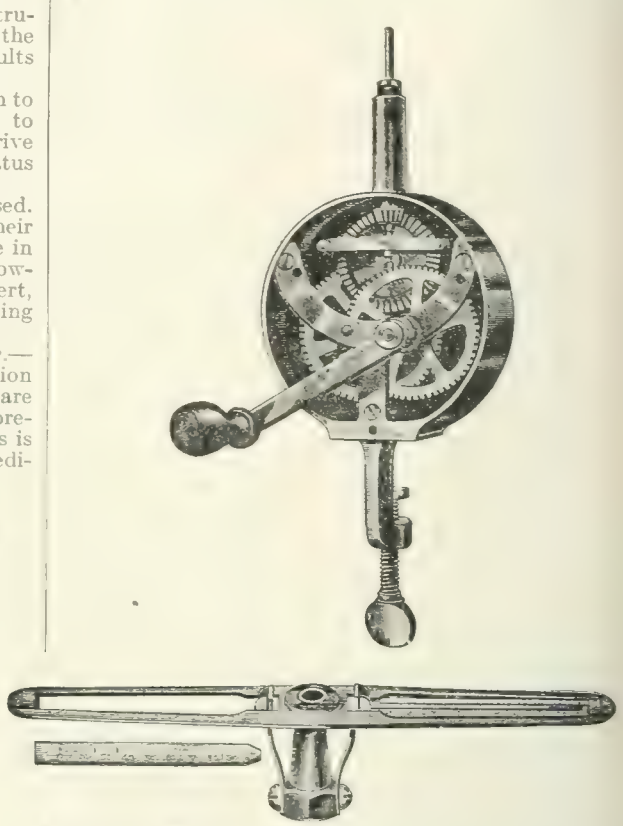


FIG. 768.—The Daland Hematocrit. (From Simon's "Clinical Diagnosis.")

By counting the blood corpuscles with the Thoma and Zeiss instrument at the same time that the blood is subjected to the centrifuge, markings to express this count may be made upon the glass tube containing the column of corpuscles.

The instrument for this method of counting is known as the hematocrit (αἷμα, blood; κριτης, a separator or discerner), blood separator. Hedin's instrument was among the first devised for this purpose (Fig. 767).

In using this instrument the blood is sucked into a capillary tube together with a 2.5 per cent. bichromate of potassium solution or Müller's* fluid, to prevent clotting, and the tube placed in the limb of the centrifuge. The wheel is then revolved for a fixed time at a fixed number of revolutions (fifty to seventy seconds with the instrument here represented), when the red corpuscles will be found arranged as a sediment at the distal extremity of the tube, with a layer of white cells next, and above the white cells, again, the diluting fluid and serum. This instrument has been simplified very much by Judson Daland of Philadelphia, working in von Jaksch's clinic (Fig. 769). By comparing the cuts (Figs. 767, 768) it will be observed

* Müller's fluid: Potassium bichromate, 2.5; sodium sulphate, 1.0; distilled water, 100.

how much simpler the latter is, the principle in both, however, being the same.

An instrument (as shown in Fig. 770) is now upon the market for the attachment of tubes for testing blood, urine, or milk. In using the Daland instrument no preservative fluid (bichromate of potassium or Muller's fluid) is employed—a questionable omission.

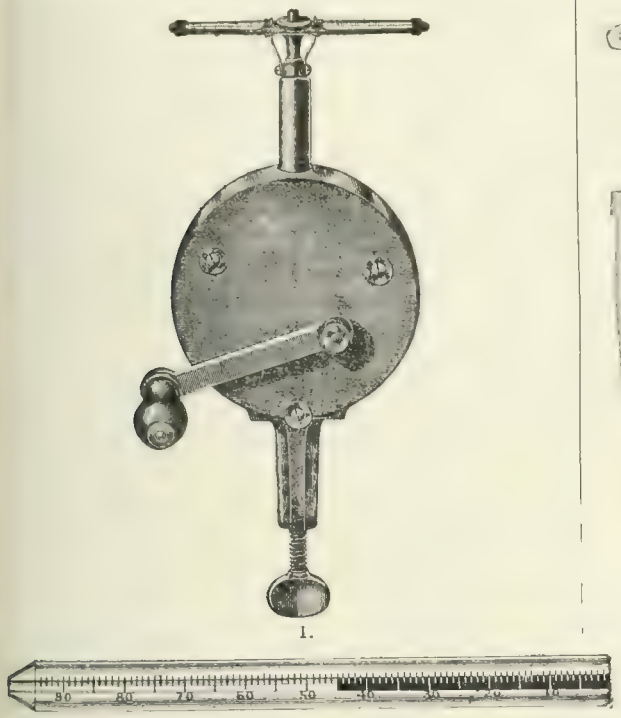


Fig. 769.—Daland's Hematocrit. 1, The centrifuge with cross piece containing capillary graduated tubes in place; 2, capillary graduated tube (magnified) containing blood. (From Simon's "Clinical Diagnosis.")

The instrument is operated as follows: A *large* puncture is made in the lobe of the ear in the usual way. A rubber tube is attached to the capillary tube and blood sucked up, *more than is required to fill the tube.* The index-finger (with a little vaseline to prevent blood from adhering to it) is placed on the far end of the capillary tube to prevent the blood from escaping, and the rubber tube is removed. The excess of blood is wiped away from the end to which the rubber tubing was attached. The capillary tube is now placed in one arm of the machine and an empty tube to balance placed in the opposite arm; then the handle of the instrument is revolved for two or three minutes. These instruments differ in the number of revolutions which they make, and each instrument should be tested to ascertain how many times it is necessary to turn the large handle in order to throw down the corpuscles so completely *that no further revolving influences them.* It is therefore impossible to give any general rule for the number of revolutions necessary beyond saying that about 4,000 revolutions of the cross-bar to the minute should be the basis upon which to calculate. By noting the number of revolutions made by the cross-bar to every single revolution of the handle this calculation can be readily made for each machine. The test, however, as stated above, is the complete precipitation of the corpuscles. The capillary tube is then removed and the column of corpuscles noted, the count being according to the figures 2, 3, 4, 5, 6, etc., in millions opposite which the top of the column is found to be. (See Fig. 769.)

The late Dr. J. Metcalfe Polk, working in the clinical laboratory at the Cornell University Medical School, made for the writer systematic observations upon the hematocrit, and compared his results with those obtained with the Thoma and Zeiss blood-counting

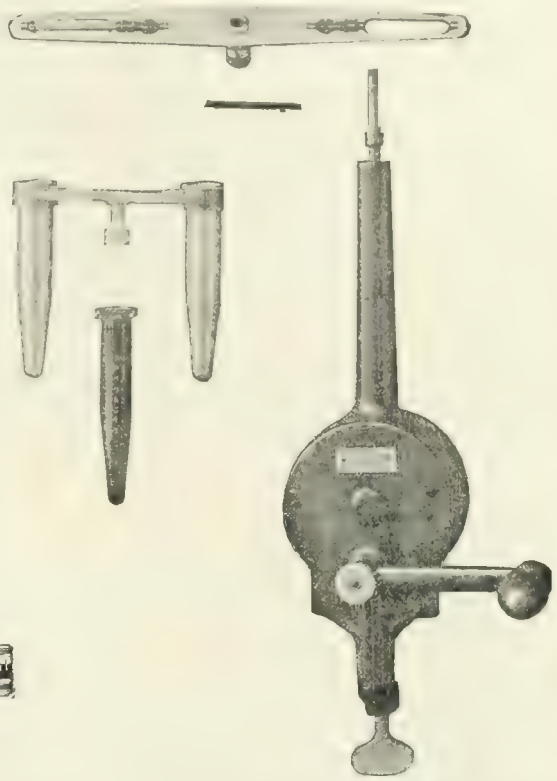


Fig. 770.—Daland's Hematocrit. With attachment for urine tubes as well as blood tubes.

apparatus. The instrument upon which these observations were made is that shown in Fig. 770. The following were Dr. Polk's results:

1	2	3	4	5	
Case.	Time.	Revolution of beam.	Reading of hematocrit.	Thoma-Zeiss count.	Remarks.
I.....	1st min.. 2d min..	2,581 2,900	7,000,000	5,056,000	
	1 min... 30 sec..	5,075 1,450	5,200,000		
	1 min... 1 min..	4,500 4,200	5,100,000		
II..	1st min 2d min	3,480 2,900	3,700,000	4,215,000	
	1st min. 2d min..	1,350 2,900	3,900,000		Spot of corpuscles in serum at 75

1	2	3	4	5	
Case.	Time.	Revolution of beam.	Reading of hematocrit.	Thoma-Zeiss count.	Remarks.
III....	1st min..	4,490			
	35 sec...	1,500	4,900,000	4,748,000	
	1st min..	4,580			Two specks of corpuscles in serum; edge at reading point ragged.
	2d min..	2,900	4,950,000		
IV	1st min..	4,300			
	2d min	4,200	4,500,000	4,960,000	
	1st min..	3,770			Corpuscles not all thrown down. Two spots in serum.
	2d min..	3,625	4,700,000		
V.....	1st min	3,200			
	2d min..	3,480			
	3d min..	3,200	5,300,000	4,852,000	
	1st min..	3,770			
	2d min..	3,770			
	3d min	3,770			
	4th min..	3,770	5,200,000		
	1st min..	5,075			
	35 sec...	1,405	5,500,000		
VI	1st min..	4,350			
	2d min	3,770	4,100,000	4,068,000	
	1st min..	4,060			Spot of corpuscles from 43 to 45.
	2d min..	3,770	4,200,000		
VII	1st min..	4,060			Spot of corpuscles 44 to 45.
	2d min..	4,030	3,650,000	3,976,000	
	1st min..	4,060			
	2d min..	3,770	3,500,000		
VIII...	1st min..	4,060			
	2d min..	4,030	3,150,000	2,564,000	
	1st min..	3,770			From 31 to 34, corpuscles thin, but column read at 34.
	2d min..	3,900	3,400,000		
IX	1st min..	4,030			
	2d min..	3,900	3,000,000	2,900,000	
	1st min..	3,900			
	2d min	3,770	3,200,000		
X	1st min..	4,030			Spot of corpuscles from 62 to 63.
	2d min..	3,800	6,000,000	4,928,000	
	1st min..	4,100			
	2d min..	3,625	5,200,000		
XI.	1st min..	4,060			Corpuscles thin from 42 to 44 1/2.
	2d min..	4,060	4,450,000	4,504,000	
	1st min..	4,350			Corpuscles thin from 41 to 42.
	2d min..	4,090	4,200,000		
XII....	1st min..	4,046			
	2d min..	4,046	4,600,000	5,088,000	
	1st min..	3,800			Corpuscles thin from 46 to 48.
	2d min..	3,770	4,800,000		
XIII...	1st min..	3,625			Case of marked jaundice. Several counts made by different people, about same results.
	2d min	3,480	3,600,000	4,624,000	
	1st min..	4,060			
	2d min..	4,150	3,700,000	4,350,000	
XIV	1st min..	4,090			
	2d min..	3,960	4,900,000	4,968,000	
	1st min..	4,060			
	2d min	4,060	4,600,000		
XV....	1st min..	4,060			
	2d min	3,950	4,200,000	4,920,000	
	1st min..	4,060			
	2d min..	3,900	4,700,000		
XVI...	1st min..	4,060			
	2d min..	4,060	4,100,000	4,472,000	
	1st min..	4,060			
	2d min..	4,060	3,700,000		
XVII...	1st min..	4,060			
	2d min..	4,090	2,800,000	2,570,000	Per self.
	1st min..	4,060			
	2d min..	3,770	2,600,000	2,650,000	Per Dr. Brown
XVIII..	1st min..	4,070			
	2d min..	3,900	1,800,000	2,200,000	Per self.
	1st min..	4,060			
	2d min	3,770	2,000,000	2,350,000	Per Dr. Brown.
XIX...	1st min..	4,060			
	2d min..	4,060	4,400,000	4,900,000	
	1st min..	4,060			
	2d min..	4,060	4,100,000		
XX	1st min..	4,060			
	2d min..	4,060	5,000,000	4,864,000	Per Dr. Scott.
	1st min..	4,060			
	2d min..	4,060	5,200,000	4,656,000	Per self.

The results of Dr. Polk's work were as follows: In revolving the handle of the hematocrit the number of revolutions per minute was counted by the watch. There was no stop between the first and second minutes as indicated under the time column. The number of revolutions above a certain number, say 3,900, means very little, as it is impossible to maintain a uniform number per five seconds throughout the minute and a half or two minutes, as the case may be. If at any time the handle is turned with extra violence for ten or twenty seconds in one specimen and not so in the second, although the number of revolutions will be the same per two minutes, the reading of the first specimen will be from 4° to 8° lower than that of the second. By looking over and comparing columns 3 and 4, the above point will be evident. Time in taking a blood count with the hematocrit, from the puncture of the finger to the reading, was on an average two minutes and forty-five seconds, or in round numbers, under three minutes; two minutes being allowed for turning the instrument. Time of a Thoma-Zeiss enumeration was over twenty-five minutes.

Time from taking the drop of blood to getting it

into the hematocrit and starting the same was never over fifteen seconds. The patient was close to the instrument. The hematocrit made so much noise that it could not be used in the wards.

Our conclusion as to the value of the hematocrit concurs with that of von Jaksch and Bleitreu, namely, that the instrument is extremely useful for routine blood work, but that in accuracy it does not equal the Thoma-Zeiss apparatus.

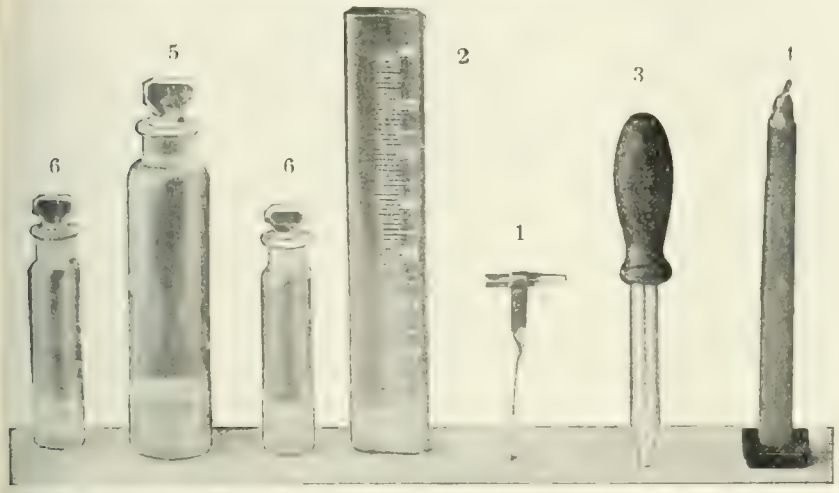


Fig. 770.—Oliver's Hemocytometer. 1, capillary tube; 2, graduated flattened receiver; 3, dropper; 4, candle and stand; 5, Bottle for Hayem's solution; 6, bottles in which to put blood and solution for subsequent examination.

Our rule was to employ the hematocrit in routine examination, and, should a case present grave anemia, to verify the count with the Thoma-Zeiss apparatus.

Enumeration of Blood Corpuscles by the Optical Method.—The third method by which the enumeration of the corpuscles is made may be termed the optical method.

The instruments used for this purpose depend for their principle upon a change in color or opacity of the blood according to its numerical value in corpuscles.

The globulimeter of Mantegazza[6] is the earliest of these instruments. The instrument consists of a receiver of glass with parallel walls. Into this receiver the blood is placed, after being diluted with ninety-six times its volume of a solution of sodium carbonate. A lighted candle is placed on the other side of the receiver, and the flame observed through the diluted blood. Blue glasses, one after another, are placed between the observer and the blood until the flame can no longer be detected. Each blue glass represents 125,000 red cells. From one to thirty glasses may be added, when by referring to the table the number of corpuscles will be ascertained.

Knowing, as we now do, that the amount of hemoglobin may be far below the number of red cells, this instrument seems to be based upon a false principle. The opacity and color of the blood are separate conditions, and bear no constant relation to the number of the corpuscles.

George Oliver[7] of London devised an instrument which he used in the preparation of his Croonian Lectures "On the Study of the Blood and Circulation." This instrument depends for its principle upon the opacity of the blood, and has nothing to do with the color or tints, so that the term tintometer, which has been applied to it, is a wrong one. The hemocytometer of Oliver (Fig. 771) consists of the following parts: (1) A capillary tube, capacity ten cubic millimeters. (2) A glass receiver whose sides are flattened so that it measures less from before backward than from side to side. The tube is about four inches in length, one inch in breadth, and about one-fourth of an inch from before backward. (3) A dropper. (4) A small candle, the size of a Christmas-tree candle. (5) Hayem's solution (for formula, see foot-note, p. 162).

The principle of the instrument is that in an opaque fluid (like blood), contained in a flattened glass receiver with vertical striations, to which is gradually added a less opaque fluid (like Hayem's solution), there develops, when such a receiver is placed between a candle flame and the eye, a point in the process of adding the less opaque fluid to the more opaque fluid at which the candle flame may be seen as a continuous bright line of light, which, before this point in dilution, is reached, is not visible and which after this point is passed no longer appears continuous, but as separate images of the candle flame. Moreover, the bright line of light consists of myriads of reflections of the candle flame produced by the vertical striations upon the glass receiver, which reflections cannot be appreciated by the eye of the observer until the opacity of the blood has been overcome by the addition of the less opaque solution. The point at which this line appears is constant for normal blood, from which constancy a unit may be established to measure blood rich or poor in corpuscles.

The instrument is used as follows: The skin is punctured in the usual way and the capillary tube applied to the drop as in using the von Fleischl hemoglobinometer (see Fig. 784), the blood entering until the tube is entirely filled. There should, of course, be no air spaces in the column of blood. Excess of

Fig. 772.—Oliver's Hemocytometer. Washing blood with Hayem's solution from capillary tube, by means of dropper, into flattened graduated receiver.

blood is wiped from off the sides of the tube, care being taken not to soak out the blood from the tube. This may be avoided either by not allowing the linen used to wipe away the excess of blood to touch the orifice of the tube, or by holding the finger over the upper end of the tube while wiping away the excess. The dropper is now filled with Hayem's solution and the capillary emptied by allowing the solution to squit through the tube, as shown in Fig. 772. This can be done by inserting the pointed end of the capillary tube into the mouth of the receiver and holding the dropper close to the blunt end of the capillary, then giving a quick pinch to the rubber end of the dropper. This sends a strong stream through the capillary and empties it almost entirely. Repeating the process will certainly clean the capillary of blood. It is not necessary to attach the dropper by a rubber connection, as shown in Oliver's illustration, for this is difficult and takes time, and allows the blood to clot in the capillary. We may now either proceed at once to the estimation, or the mixture thus made may be put into a small bottle and estimated at any time within twelve hours. Thus several such mixtures may be made in the course of the morning's round and placed in bottles properly labelled, the estimation being made when the physician returns to his office or laboratory. Or the specimens may be sent by mail, if the distance be not such as to require more than twelve hours in transportation. These are distinct advantages over the Thoma-Zeiss instrument.

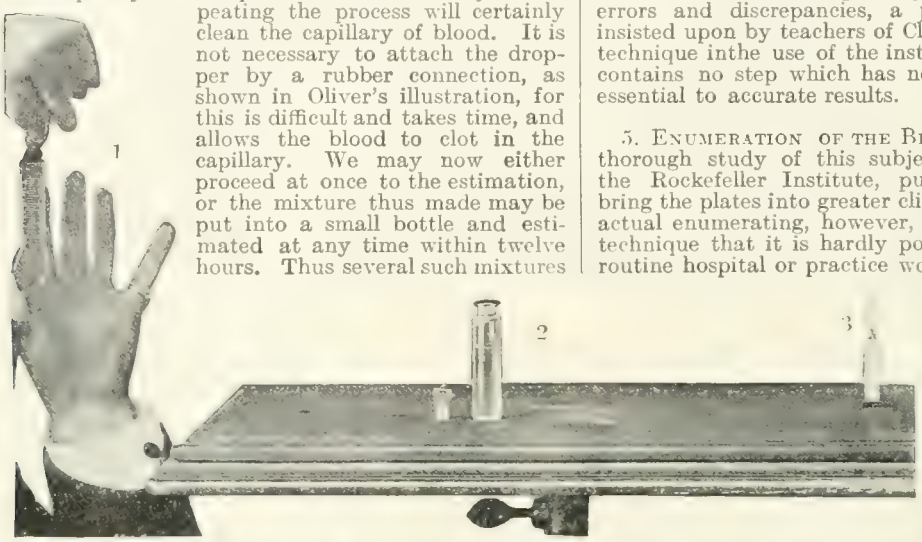


Fig. 773. Oliver's Hemocytometer. Watching for that degree of opacity at which candle flame will be seen as transverse bright line across flattened receiver. 1. Holding flattened receiver close to eye, between thumb and forefinger of left hand, while adding Hayem's solution from dropper with right hand; 2, bottle holding Hayem's solution; 3, candle ten feet away from observer and on a level with observer's eye.

If a candle flame ten feet away be viewed in a perfectly dark room through the receiver held as shown in Fig. 773, the receiver containing blood and Hayem's solution up to the 10 mark, for example, owing to the opacity of the mixture the flame will appear as a faint diffuse light. If now we add little by little the Hayem's solution, as the opacity becomes less the flame will become clearer, and will be caught by the vertical striations on the receiver, which act as minute mirrors to reflect the flame as a continuous line of light. When the mixture has reached that degree of opacity which allows of this phenomenon we read off the upper limit of the fluid in the receiver: 100 on the scale represents 5,000,000; 80, 4,000,000; *i.e.* 20 on the scale indicates 1,000,000 corpuscles.

By moving the receiver slightly from side to side, and from before backward, the line may be detected at the sides a little before it extends across the receiver, a signal to the observer to add the solution cautiously drop by drop. Before the fluid has reached the height at which the line appears continuous the line is noticed to be blurred. As we add more fluid than is necessary to produce the continuous line, the line ceases to be a continuous one and becomes a series of minute but separate images of the candle flame. The point, therefore, at which the reading should be made is *after the line ceases to be blurred and before separate images of the flame can be observed.* The candle should be at least ten feet away and should be not larger than the ordinary Christmas-tree candle. The receiver should be held in the right hand and the thumb pressed well into the side of the nose so as to shut off all diffused light, as shown in Fig. 773.

Of all the apparatus here described the Thoma and Zeiss instrument has become the most popular and in this common use of one instrument there is a very great advantage to accuracy and uniformity in blood statistics. The constant use of one instrument, moreover, tends to perfect the technique. The instrument must, nevertheless, be accurately used, for carelessness even of slight degree leads to enormous errors and discrepancies, a point not sufficiently insisted upon by teachers of Clinical Pathology. The technique inthe use of the instrument here described contains no step which has not been proven to be essential to accurate results.

5. Enumeration of the Blood Plates.—After a thorough study of this subject, Pratt,[2] working in the Rockefeller Institute, published results which bring the plates into greater clinical importance. The actual enumerating, however, requires such delicate technique that it is hardly possible to employ it in routine hospital or practice work. Pratt's review of the literature shows that observers have varied in their enumeration of the plates per centimeter between 200,000 and 778,000. These great variations Pratt attributes to, (1) mistaking fragments of erythrocytes (Arnold bodies) for plates; (2) the failure to count the plates which have adhered to a glass counting pipette; (3) the failure to observe plates floating in a counting chamber which is too deep and which requires too long for the plates to settle to the counting field; (4) The unsatisfactory preserving fluids.

To overcome these he recommends the following for the preservative fluid.

Sodium metaphosphate (Merck)	2 grams.
Sodium chloride	0.9 gram.
Distilled water	100 c.c.

A few cubic centimeters of this solution are poured into a watch glass, the ear is cleansed with soap and water, alcohol and ether, and stabbed deep enough for blood to flow freely. A sterilized platinum loop is now filled with the preservative fluid and the drop of blood touched with it so that there is about three of fluid to one of blood. This is now transferred to a cover slip and further diluted if desired and the slip at once placed on a slide. It is not necessary to stir the specimen with the loop. Two such preparations should be thus prepared in order to determine if there is great variation between the two, a condition calling for the taking of other specimens. An oil immersion lens with a Leitz three ocular is now employed and the ratio of plates to erythrocytes determined. In order to do this it is necessary to make an erythrocyte count with the Thoma-Zeiss apparatus. The plates in the fresh specimen can be counted either with the Ehrlich ocular (see Fig. 802), or with a square diaphragm made of paper or cardboard. Pratt emphasizes the necessity for absolute cleanliness of the slide and cover slip and recommends that these be tested with the water drop which will

spread in a uniformly thin layer if the glass is sufficiently clean.

By this method Pratt obtained in twenty-five cases a maximum count of 725,000, minimum 226,000 and an average of 469,000.

6. What can be Learned from Corpuscle Counting.—1. By this means oligocythemia (cell decrease) and polycythemia (cell excess) can be determined. The anemias (chlorosis excepted) and the polycythemias are thus diagnosed.

2. By this means also leukemia and leucocytosis can be detected. In order to differentiate chlorotic anemia and to determine the type of white cell increase present it is necessary to estimate the hemoglobin and to stain the blood. The first of these we will now consider.

III. Hemoglobin.

1. Its Derivatives and their Relative Clinical Importance.—Normally the hemoglobin is contained wholly within the red cell. These cells in the arterial stream have a full burden of oxygen in the form of oxyhemoglobin, whereas in the venous stream

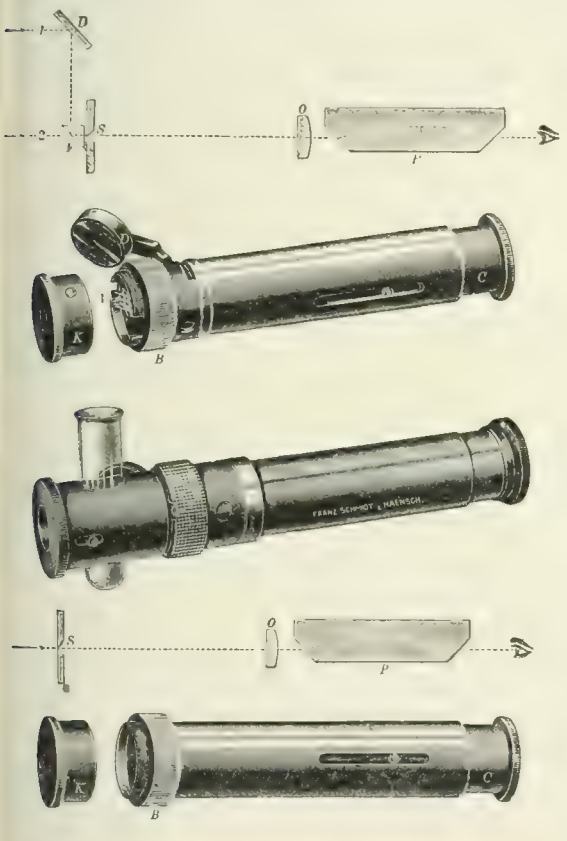


Fig. 774.—Three Forms of Simple Hand Spectroscope.

hemoglobin alone is present in the red cell. In obtaining blood from the capillaries of the skin of the ear or finger, the arterial and venous blood is more or less equally represented. The specimen thus obtained will therefore be a mixture of oxyhemoglobin and hemoglobin. The oxygen is very loosely combined with the hemoglobin and the hemoglobin can be separated readily from the red cells by the addition of water. The first of these facts gives to hemoglobin its vital importance in the work of nourishing the tissues and the second is that which enables us to determine approximately and relatively, *not absolutely*, the amount present in a given case.

2. The Spectroscope.—In exceptional cases only are we called upon to determine *clinically* the chemical derivatives of hemoglobin. For this purpose the hand spectroscope (Fig. 774) is very satisfactory. The Heeley spectroscope is the most practical for clinical and general laboratory work. For the absorption bands as seen in the spectra of the more common substances see Plate XIV.

3. Quantitative (Relative) Estimation of Hemoglobin. *Apparatus and Technique.*—The task of estimating the amount of hemoglobin has long been an unsatisfactory one, because all methods, excepting only the specific-gravity method, depend upon the comparison of colors, a subject upon which nearly all indiviuals differ, and upon the degree of opacity, which is supposed to vary with the amount of hemoglobin, a supposition by no means proven.

The instruments group themselves into three classes, as follows:

A. *Opacity Methods*	
1. Bizzozero's chromocytometer.	Based upon the supposition that the amount of hemoglobin varies with the degree of opacity
2. Henoque's hematoscope	
B. *Color Methods*	
1. Gowers hemoglobinometer	Based upon the supposition that the amount of hemoglobin varies with intensity of color.
2. Fleischl hemoglobinometer	
3. Fleischl-Miescher hemoglobinometer	
4. Taylor hemoglobinometer	
5. Oliver hemoglobinometer	
6. Tallqvist hemoglobinometer	
7. Dare hemoglobinometer	
8. Sahli hemoglobinometer	
C. *Specific-gravity Method*	
1. Hammerschlag's method	Based upon the supposition that the amount of hemoglobin varies with the specific gravity.
2. Roy's method	

A. *Opacity Methods.*—1. *The Chromocytometer of Bizzozero*[8] depends for its principle upon the supposition that the opacity of the blood varies with the amount of hemoglobin.

The instrument may also be used to estimate the number of red cells, but its value for this purpose is doubtful, for it is based in this application, as is Mantegazza's instrument, upon the false supposition that the opacity of the blood varies with the number of cells contained.

When using it as a cytometer, instead of adding colored glasses as in Mantegazza's instrument (see p. 182), Bizzozero introduces more and more blood until the *opacity* of the blood gives rise to partial obscuring of a candle flame. The thickness of the layer of blood producing this condition is then measured by comparison with standard observations, and the amount of hemoglobin estimated accordingly.

The chromocytometer of Bizzozero is an instrument intended primarily for the estimation of hemoglobin. The name is misleading. The instrument is so called because the amount of hemoglobin is ascertained by two methods: (1) By observing the degree of opacity produced by the hemoglobin *unremoved* from the corpuscle, and therefore the actual corpuscular value of hemoglobin—in which application it is called a *cytometer* (κύτος, a cell, + μέτρον, a measure). It does not number the corpuscles, as at first the name seems to imply. (2) By observing the color produced by the hemoglobin removed (dissolved) from the corpuscle and comparing this color with a standard colored glass—in which application it is called a chromometer (χρῶμα, color, + μέτρον, a measure). Its application as a hemocytometer is a wrong one, as already stated.

As a Cytometer (term understood as above described). *Principle.*—If a fixed quantity of blood be mixed with a fixed quantity of preserving fluid (saline solution), and the mixture placed in a receiver,

and a candle flame viewed through the mixture in a dark room, then, according to the amount of hemoglobin and the amount of the mixture used, the flame of the candle will either be seen or will not be seen. By observing the amount of this mixture necessary, in normal cases, partially to obscure the candle, and calling this 100, we can, as more or less of such a mixture is required in pathological cases, ascertain the decrease or increase in the amount of hemoglobin.

The instrument consists of a well which *connects* with a chamber closed at both ends with colorless

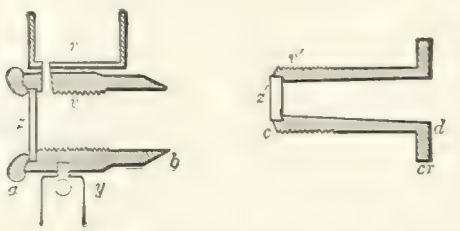


Fig. 775.—Diagram Showing Construction of Bizzozero's Chromocytometer. *r*, Well connecting with *b*, chamber formed by *b'*, which screws into *r*; *z* and *z'*, glass windows.

glass. The chamber consists of two pieces of metal, one screwing into the other. These are hollowed out so as to form the chamber within (Fig. 775). By screwing or unscrewing one of these pieces the dimensions of the chamber may be decreased or increased. It will be seen that if diluted blood be placed in the well which connects with this chamber, the blood will flow into the chamber through this connection. But only just so much blood will flow into the chamber as is allowed by unscrewing the outer screw. When the outer portion of the instrument is screwed home (Fig. 777) no fluid at all enters the space between the screws—in other words, the chamber is then obliterated. Now by unscrewing or screwing the piece of metal which fits into the other piece and which, together with its fellow, forms the chamber, we can increase or decrease the amount of fluid in the space between the screws.

(1) Suppose now the two pieces of metal to be completely screwed together, so that no space exists between them, the scale then stands at 0. (2) We fill the well (Figs. 775–777,*r*) with fifty parts of normal saline solution to one part of blood; or, to be more accurate, by means of a pipette we mix ten cubic millimeters of blood with 0.5 c.c. saline solution (0.75 gram of NaCl in 100 c.c. water), which preserves the corpuscles. (3) A candle is placed in a dark room about four feet away from the observer. (4) The instrument is held by the left hand and close to the right eye, opposite the candle. (5) The two ends of the chamber, it will be remembered, have glass windows, so that the candle flame will be clearly seen. (6) With the right hand the pieces of the metal are slowly unscrewed, which allows the blood to flow from the well into the chamber. (7) As we introduce more

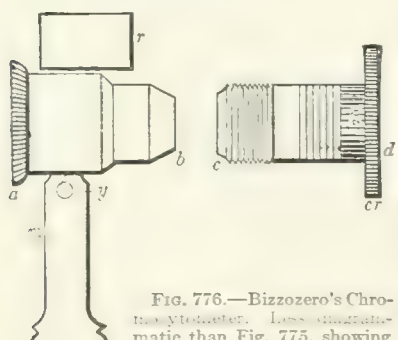


Fig. 776.—Bizzozero's Chromocytometer. Less diagrammatic than Fig. 775, showing side view. The outer screw unattached. Lettering same as in Fig. 775. *m*, Handle. From von Jaksch's "Clinical Diagnosis.")

and more fluid into the chamber, however, a degree of opacity must be reached at which the candle flame will be almost or wholly obscured. This is just what occurs. By observing the degree of unscrewing, so to speak, necessary to produce this opacity for normal blood, we obtain a unit with which pathological blood may be compared. By means of the table given below the amount of hemoglobin may then be ascertained.

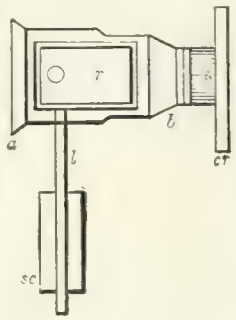


Fig. 777.—Bizzozero's Chromocytometer. Screws completely screwed together, obliterating chamber. Well viewed from above. In this position one looks into the well. The round ring represents the connection between well and chamber. From von Jaksch's "Clinical Diagnosis.")

When the space between the glass windows is obliterated by screwing the outer portion home, the index on the scale stands at 0. One complete rotation of the screw produces a space in the instrument measuring 0.5 millimeter. This is therefore the thickness of the contained solution of blood. One complete turn, however, renders the candle flame decidedly less visible. This complete rotation is therefore subdivided on the scale into 0.02 millimeters, twenty-five such divisions ($0.02 \times 25 = 0.5$) constituting one complete revolution, and fifty such subdivisions ($0.02 \times 50 = 1.0$) constituting 1.0 on the scale. From a number of observations (as stated by von Jaksch) upon the blood of healthy individuals, the outlines of the candle flame are distinctly seen through a layer of blood $\frac{1}{100}$ millimeter thick = 1.0.

This, then, is the unit; *increase* of this number means *decrease* in amount of hemoglobin. For if we must increase the thickness of the stratum of blood in order to obscure the candle flame, it indicates that the fluid is poor in coloring matter, and that an excess is required to produce dimness of the candle flame.

Scale.	Hemoglobin.	Scale.	Hemoglobin.
110 represents	100.0	170 represents	64.7
120 represents	91.6	180 represents	61.1
130 represents	84.6	190 represents	57.9
140 represents	78.5	200 represents	55.0
150 represents	73.3	210 represents	52.4
160 represents	68.7	220 represents	50.0

If one has not this table at hand the reading can be readily interpreted by remembering that 110 = 100. Suppose, for example, the reading to be 160 on the scale; then:

$$160 : 110 :: 160 : x$$
$$100 \times 100 \div 160 = 68.7$$

As a Chromometer (term understood as above described).—In addition to the parts of the instrument as already enumerated, there is a colored glass (see Fig. 778). This is introduced on one side of the instrument so that the colored glass and the glass windows of the instrument are *side by side*, as would be the case with a pair of opera glasses if one side were to consist of only the eyepiece, and that with a colored glass in it. In this use of the instrument, moreover, the hemoglobin is dissolved out with water in preparing the blood for observation.

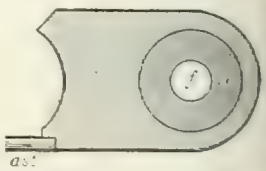
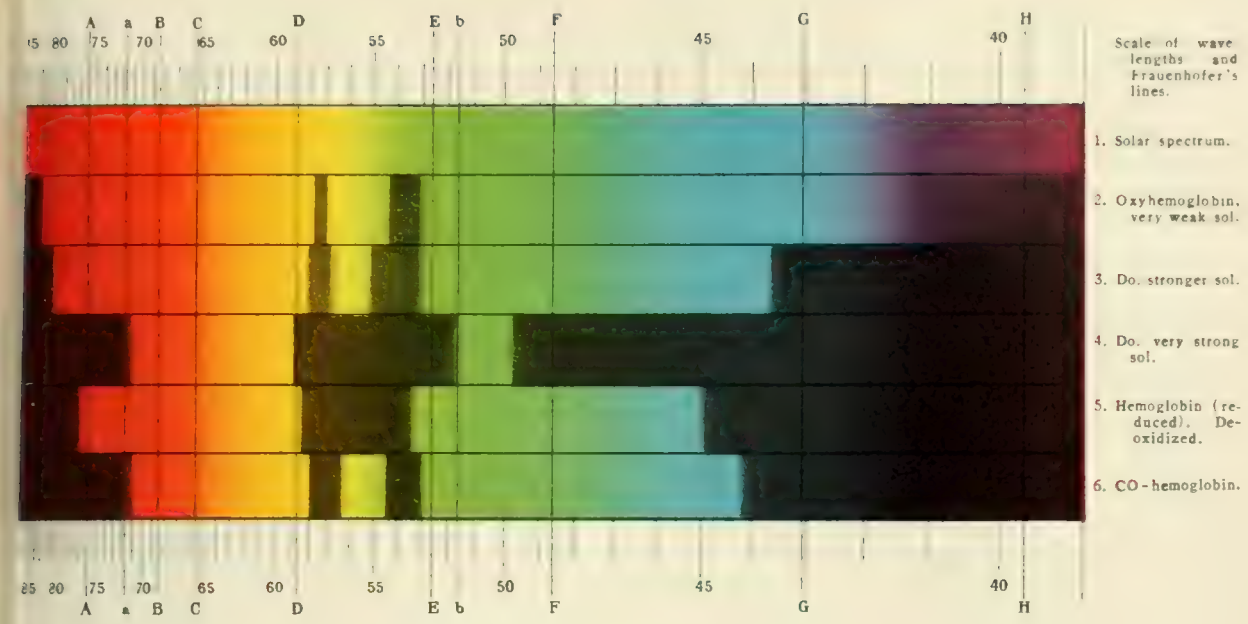
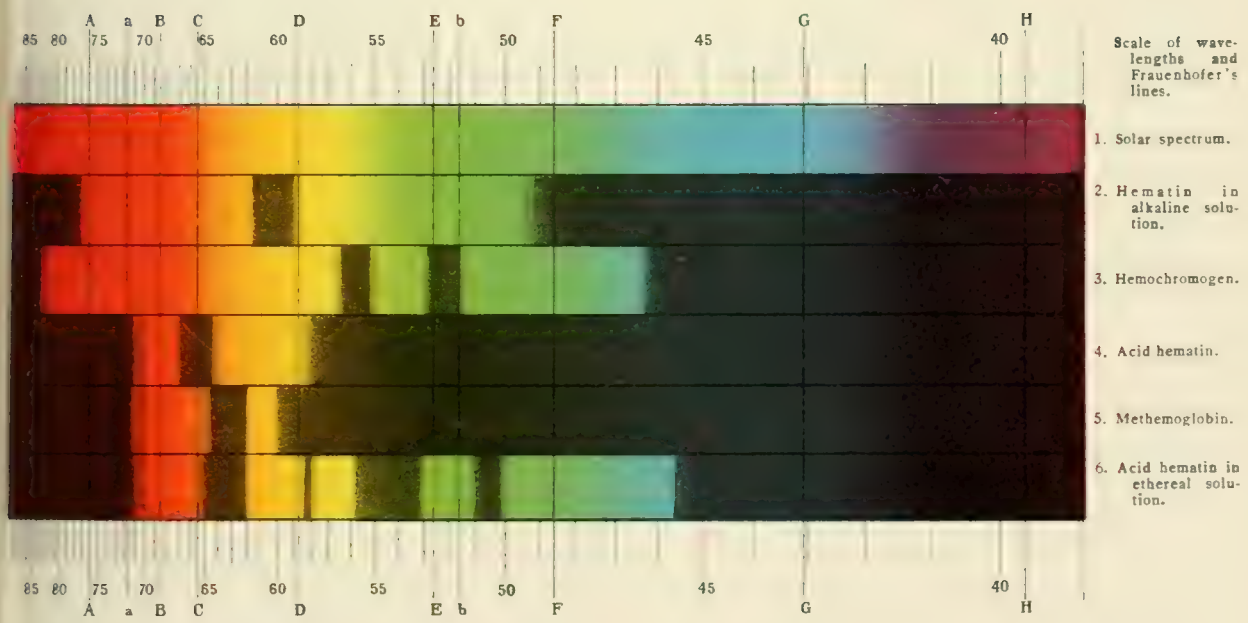


Fig. 778.—Bizzozero's Chromocytometer. Frame holding tinted glass. This is placed by the side of the screw of the main apparatus. *f*, Tinted glass; *l*, frame; *ast*, rod which passes through hole *y* in handle *m* of Fig. 776.

Principle.—If a glass colored to correspond with a definite solution of hemoglobin be placed before a


A a B C D E b F G H
85 80 75 70 65 60 55 50 45 40
Scale of wave lengths and Frauenhofer's lines.
1. Solar spectrum.
2. Oxyhemoglobin, very weak sol.
3. Do. stronger sol.
4. Do. very strong sol.
5. Hemoglobin (reduced). Deoxidized.
6. CO-hemoglobin.


A a B C D E b F G H
85 80 75 70 65 60 55 50 45 40
Scale of wave-lengths and Frauenhofer's lines.
1. Solar spectrum.
2. Hematin in alkaline solution.
3. Hemochromogen.
4. Acid hematin.
5. Methemoglobin.
6. Acid hematin in ethereal solution.

otice the degree of intensity, in the upper spectrum, of the D, E bands in the varying strengths of moglobin in 2, 3 and 4. Dilution can be carried to the point where only one faint band appears, usually D.

BLOOD SPECTRA

From Lyle's Physiology

bright light (the sky) and beside a solution of hemoglobin to be tested, the color of the tinted glass and that of the solution of hemoglobin will be found to differ. If, however, more or less of the solution be added, a point will be reached at which these colors correspond. By noting the amount of solution required to make these colors exactly correspond a scale may be made by which the amount of hemoglobin may be estimated.

Given a tinted glass which corresponds in color with a known solution of hemoglobin. Given a known quantity of blood (ten cubic millimeters) with a known quantity of water (0.5 c.c.). If the blood to be tested contains much coloring matter (hemoglobin), it will be necessary to add but little of the solution in order to make the colors correspond; if it contains little coloring matter, much will be required to make these colors correspond. These quantities are noted and compared with a scale, each quantity of fluid corresponding with a percentage of hemoglobin.

By referring to Figs. 776 and 777, the workings of the apparatus will be readily understood.

The colored glass is not of the same intensity of color in every instrument, so that the glass must be tested for each instrument.

The test is performed in the following way: Normal blood is tested, and is found to be, by the cytometer method, 110, and by the chromometer, say 130. One

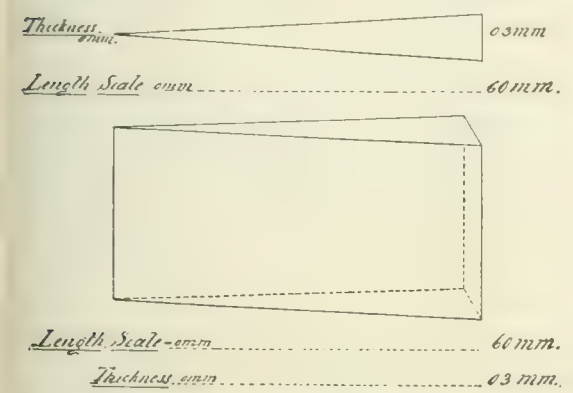


Fig. 779.—Henocque's Hematoscope. Diagram showing dimensions of prismatic space formed by plates of glass.

hundred and ten of the cytometer equals 100 hemoglobin. For this glass, then, 130 also equals 100.

As in the case of the cytometer method, we construct a table from these relations. Suppose the reading with the chromometer to be 190.

$$190 : 100 :: 130 : x$$
$$100 \times 130 \div 190 = 68.4.$$

After a brief experience in using this instrument the author is inclined to commend it.

2. *Henocque's Hematoscope.*—This instrument also depends for its principle upon the supposition that the amount of hemoglobin varies with the degree of opacity of the blood. In this instrument, in addition to the degree of opacity, the quantity of oxyhemoglobin can be ascertained by means of the spectroscope. For this purpose the hand spectroscope illustrated above (Fig. 774) can be used but as von Jaksch states, there is a "difference of opinion as to when precisely the spectrum is formed," which makes the conclusion drawn from the use of the instrument "always somewhat arbitrary."

The instrument consists of two plates of glass, one placed above the other so as to enclose between them a prismatic space. The dimensions of this space are accurately stated and are the same for every instrument. These plates of glass are in contact at one end,

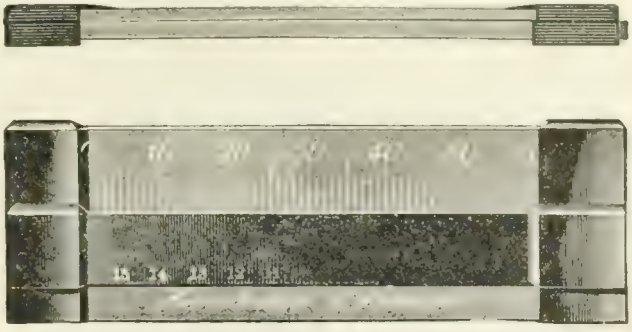


Fig. 780.—Henocque's Hematoscope Filled with Blood. (From von Jaksch's "Clinical Diagnosis.")

forming the apex of the prismatic space. The scale of measurement at this end is therefore 0.

At the other end the glass plates are separated by a distance of 0.3 millimeters, forming the base of the prismatic space. By referring to the diagram (Fig. 779) and illustrations (Figs. 780 and 781), this arrangement will be readily understood.

The scale upon the glass is marked from 0 to 60, as observed in Fig. 780.

There are two methods of using the instrument.

(1) The first method is based upon the supposition that varying opacity of the blood differs according to varying quantity of hemoglobin, so that by observing the former the latter may be estimated.

To use the instrument upon this basis, puncture is made in the skin in the usual way and the drop brought to the orifice of the prismatic space, which, from its dimensions, will be observed to be capillary. The blood on this account passes readily into the space without being diluted, an advantage over the dilution methods.

About six drops of blood are necessary to fill the space. Excess is wiped away.

In addition to the apparatus already described, there is an enameled plate, as seen in Fig. 781.

This plate is placed behind the prismatic layer of blood, so that the figures 0, 10, 20, etc., correspond with the like figures on the glass plate of the hematoscope. At the apex end of the prism, and therefore at the thinnest portion of the layer of blood, the marking on this enameled plate will be visible; but as the eye passes toward the thicker portion of the prism of blood a point will be reached at which the marking can no longer be seen. If the blood tested be rich in hemoglobin the opacity will be greater, and therefore the point in the series 15, 14, 13, 12, etc., at which this

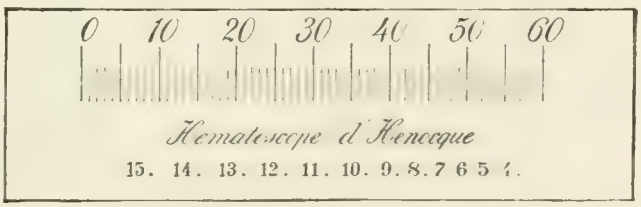


Fig. 781.—Enamelled Plate Used with Henocque's Hematoscope. (From von Jaksch's "Clinical Diagnosis.")

obscuring occurs will be higher, say 11 or 12, as seen in the illustration. If, on the other hand, the blood be poor in hemoglobin, the opacity will be corre-

spondingly less, and we shall be able to see the figures 10, 9, 8, etc., in the series.

One hundred grams of normal blood contain fourteen grams of oxyhemoglobin. These figures, therefore, indicate the number of grams of oxyhemoglobin in 100 grams of blood. For this use the author commends the instrument.

(2) The second method is based upon the supposition that the richer the blood is in hemoglobin the thicker will be the layer necessary to detect through the spectroscope the characteristic bands of oxyhemoglobin. By noting the thickness in normal blood at which the oxyhemoglobin spectrum occurs, a scale may be made with which deviations from the normal may be measured. The apparatus, with the exception of the enamel plate, is used as before.

The prism is fitted in front of a spectroscope and is turned until the oxyhemoglobin bands appear, when this point is noted on the scale. With normal blood the oxyhemoglobin spectrum is seen opposite 14 of the millimeter scale. Now for every millimeter on the scale the thickness of the prismatic space increases 0.005 millimeter. This can be demonstrated by multiplying 0.005 by 60, the length of the scale; the result is 0.3 millimeter, the thickness of the prism at its base, *i.e.* at the sixty millimeter end. As, therefore, for normal blood the spectrum appears at 14 on the millimeter scale, we determine the thickness of blood required to produce this spectrum by multiplying 14 mm. $\times$ 0.05 mm. = 0.07 mm.

This, then, is a unit; it is the thickness of normal blood required to produce the oxyhemoglobin spectrum.

Suppose a specimen of blood produces the oxyhemoglobin bands at 40 on the millimeter scale. The thickness of this specimen would be 40 mm. $\times$ 0.005 mm. = 0.2 mm. Then:

$$\frac{0.07 \cdot 14}{0.2} = x = 4.9 \text{ grams of hemoglobin in 100 grams of blood.}$$

An equation for any reading is the following:

$$14 : (y \times 0.005) :: 0.07 : x$$

in which

y = reading on the scale.

0.005 = thickness of prism for each millimeter division on the scale.

0.07 = thickness of layer of normal blood by which oxyhemoglobin spectrum is produced—*i.e.* at 14 on the scale ($14 \times 0.005 = 0.07$).

14 = quantity of oxyhemoglobin in 100 grams of normal blood.

From these calculations one can make for himself a table which will at once give him the amount of the hemoglobin for any reading on the scale. Thus beginning with 5 on the millimeter scale, and substituting it for y in the equation, we get the following:

$$(5 \times 0.005) \times 0.07 \div 14 = 12.5.$$

Therefore five millimeters of the scale = 12.5 grams hemoglobin in 100 grams of blood.

If we substitute in the same way, 10, 15, 20, etc., the table becomes complete.

The instrument has not been much used in this country. Since the hand spectroscope has come into common use the chief objection to this instrument ("complicated apparatus") has been removed. It is difficult to obtain a uniformity of opinion as to the exact point at which the oxyhemoglobin band appears. Beyond this statement the writer cannot express an opinion upon the value of this method.

B. *Color Methods.*—Before entering upon the description of those hemoglobinometer instruments which depend for their principle upon the comparison of colors, it would be well to quote from Lovibond's very interesting and valuable work on "Measurements of Light and Color."

"It is almost impossible," says Lovibond, "without special arrangements to arrive at a reliable judgment between two colors which are very nearly, but not quite, alike, when these are placed openly side by side. The difficulty arises from the unequal incidence of light—sometimes of the direct light, frequently of the side lights, or from both combined. The disturbing effect is so great that a slight change of position in either of the samples, or of the observer, generally reverses the first judgment.

"The same causes account for the *frequent differences of opinion between two persons* judging the same color; in fact, the color sensations of our surroundings are. . . . governed by the ever-varying conditions of light, surface, substance, texture, and chemical composition . . ."

The following are the experiments carried out by Prof. Lovibond:

"*Test-tubes Containing Colored Liquids.*—The first attempts were made with colored liquids in test-tubes of equal diameters, and by these means some useful information was obtained. The liquids, however, *soon changed color*, requiring frequent renewals; and there was always a little uncertainty concerning their exact reproduction. Also a curious inequality of color relation was found to exist between the regular increase of strata thickness and their resulting color. This prevented liquids from being suitable as standards, because some liquids increase in color depth in direct proportion to increase of strata thickness. Some increase in color in a less but regular proportion to increase of strata thickness, while others increase in a less and irregular proportion.

"Another difficulty arose from the convex surfaces of the test-tubes acting as a lens, and increasing the disturbance arising from unequal light incidence. The convexity was reduced by using larger tubes, and enclosing them in a blackened case with narrow longitudinal apertures for looking through the middle of the tubes. The results, although useful, were too unsatisfactory for systematic work.

"*Colored glass* was next tried, and long rectangular wedges in glass of different colors, with gradually graded tapers, were ground and polished for standards, while correspondingly tapered vessels were made for the liquids to be measured. These were arranged to work, at the end of the instrument, up and down at right angles before two apertures, side by side, with a fixed center line to read off the thickness of each before the aperture when a color match was made; but here also the difference of ratio between the thickness and color depth of the different colored glass and liquids proved fatal to the method.

"An incidental observation was made during these experiments concerning the difficulty of arriving at a final judgment with tapering colors, owing to one shade gradually blending into the next without a break of any kind to arrest the vision. The mental effort to arrive at a decision, under these conditions of gradual color-blending, was troublesome and vexatious in the extreme. Any person may realize this difficulty by attempting to fix a definite point by the vision in a graduated color line. I was enabled entirely to remove the difficulty by using separate glass slips for standards; the line of color decision made by each additional standard-glass slip used being a precise definition between the most minute shades.

"The effect of these partial failures enabled me more clearly to define the conditions from which successful work might be expected, which are as follows:

"*Gauged Cells.*—The cells for the liquids must have parallel transparent ends and be gauged to definite strata thickness.

"*Optical Instrument.*—The standard and sample must be viewed under equal conditions of illumination.

"*Suitable Light for Color Work.*—Considerable differences of view exist concerning the most suitable light for color work. Some authorities consider that daylight is too unreliable in composition, and that

an artificial light, such as the electric arc, is best, as being always uniform.

"Captain Abney's work and apparatus at first sight go a long way toward establishing this view. Some valid reasons, however, in my opinion, exist in favor of daylight; as it is the light to which normal vision is most accustomed and it is available without cost at a moment's notice during daylight hours, whereas artificial lights require to be worked in camera with somewhat expensive apparatus. Again,

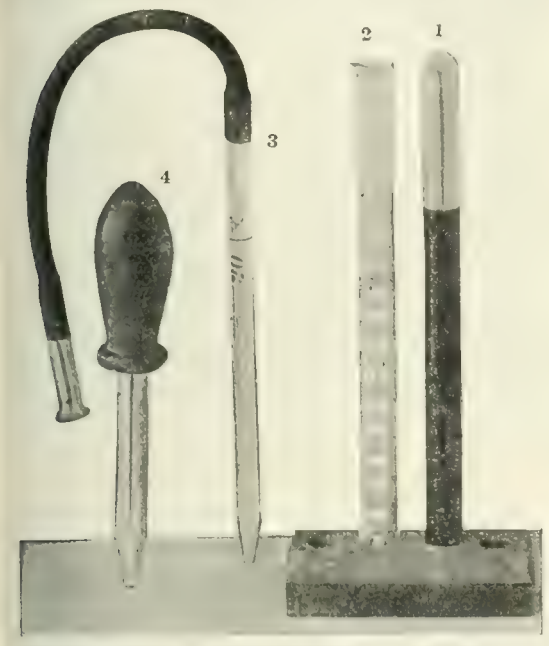


FIG. 782.—Gower's Hemoglobinometer. 3, Capillary tube for taking a definite quantity of blood; 4, dropper for adding water; 2, graduated receiver for blood and water; 1, tube containing picrocarmine, color equal to that of blood with one per cent. hemoglobin.

by far the largest proportion of artistic and commercial color work is carried on by daylight, so that measurements made by means of any other light must be transposed into terms of daylight values before reliable comparisons can be made. Without doubt the vision can work longer and with less fatigue by daylight than by intense artificial light."

From the foregoing it will be seen that liquids and colored glasses have a distinctive color value, and that any method which employs blending colors, as the colored prism of the von Fleischl apparatus or the gradually diluted blood in the Gowers instrument, presents a wider field for error than that method which employs fixed and uniform colors for comparison. Also daylight is the most reliable.

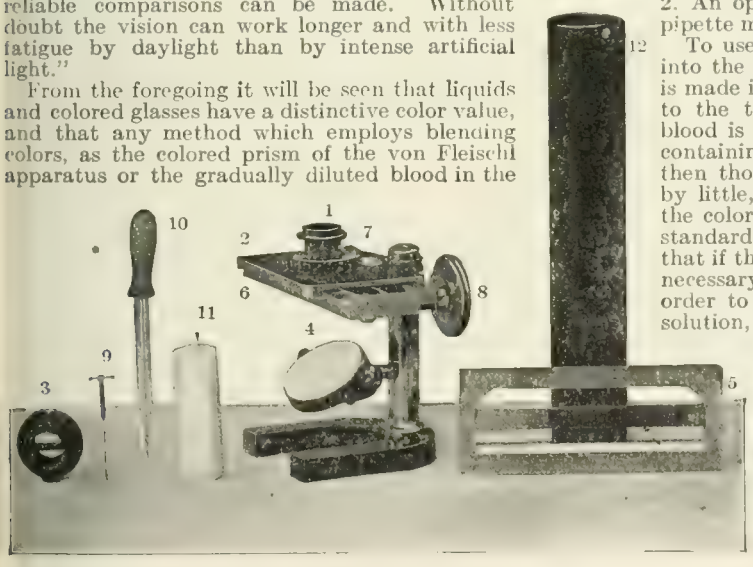


FIG. 783.—Von Fleischl's Hemoglobinometer.

1. *Gowers Hemoglobinometer.*—This instrument is one of color comparison.

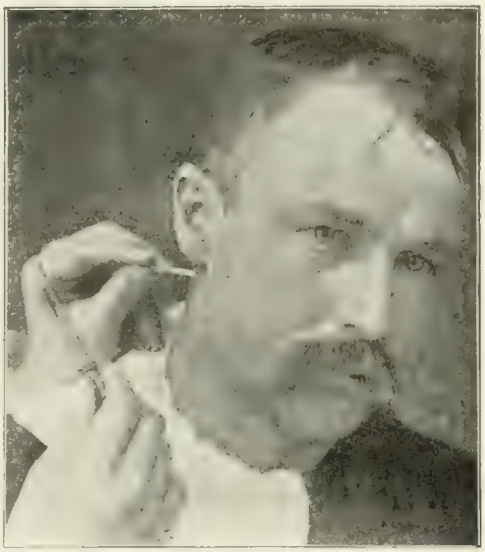


FIG. 784.—Von Fleischl's Hemoglobinometer. Taking drop of blood in capillary tube.

Principle.—If a colored fluid representing a very low percentage of hemoglobin be placed by the side of a solution of a fixed quantity of blood, to which water is added little by little, a point in the process of dilution will be reached at which the two colors correspond.

By observing the amount of diluting fluid required to bring normal blood to a corresponding color with the fixed color, a scale may be made by which deviations from the normal may be detected.

The parts of the instrument (Fig. 782) are (numbers correspond with those in cut): 1. A solution of picrocarmine-glycerin of the color of a one-per-cent. solution of normal blood, contained in a sealed tube. 2. An open tube graded from 10 to 120. 3. A pipette measuring 10 and 20 cm. 4. A dropper.

To use the instrument: A little water is put into the graduated tube. Puncture of the skin is made in the usual way, and blood drawn up to the twenty cubic millimeter mark. The blood is at once blown into the graduated tube containing the water. The blood and water are then thoroughly mixed, and more water, little by little, added by means of the dropper until the color of the diluted blood and that of the standard solution correspond. It will be seen that if the blood is rich in hemoglobin it will be necessary to add a large quantity of water in order to make it of the color of the standard solution, which represents only one per cent.

As we add more and more water, however, the column of fluid rises on the scale, and therefore indicates a high percentage of hemoglobin. In cases of anemia the correspondence will be sooner reached, and the column of fluid will stand at a lower level in the tube, and will therefore indicate a low percentage of hemoglobin.

This instrument has the advantage of being cheap as well as accurate.

The standard solution, picrocar-

mine, changes color in time, a point noted by Lovibond and by Oliver working in Lovibond's laboratory.

2. *Von Fleischl Hemometer*—or, more correctly, hemoglobinometer—depends for its principle upon the supposition that a solution of hemoglobin varies in color according to the amount of hemoglobin which it contains, and that the latter may be measured by comparison with the varying colors in a prism of glass, each degree of color corresponding to a percentage of hemoglobin.

We must keep in mind that when water is added to blood the hemoglobin is dissolved out of the corpuscles, and it is the colored solution which we are comparing, not the hemoglobin as contained in the corpuscles.

The parts of the instrument are (numbers correspond with those in illustration, Fig. 783): A stand (1) with a horseshoe base. A stage (2) with a round hole in the center for the reception of (3) a well 1.5 centimeters in depth and divided into two equal parts; the bottom of this well is closed by a piece of clear glass. Below the stage is a round reflector of plaster of Paris (4). In a metal frame is a prism of colored glass (5). On the frame opposite the apex of the prism there begins a series of figures, the first being 0 and the last, which is opposite the base of the prism, being 120. At 0 the tint of the color is the faintest, this tint increasing in intensity until it reaches maximum, 120. The frame is introduced into two tracks (6) which run below the stage. It is placed so that the colored glass prism shall pass beneath one division of the well, and the series of figures shall appear through an oval opening (7) in the stage just behind the well. By means of a rack (8) and pinion different parts of the varicolored glass prism may be made to pass along the bottom of one division of the well, and at the same time the figures indicating the color intensity of the glass at that

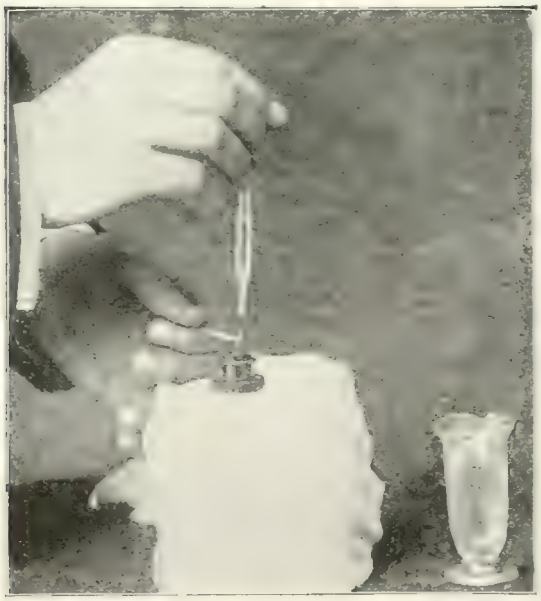


Fig. 783.—Von Fleischl's Hemoglobinometer. Washing drop of blood from capillary tube with water into one side of double well.

point will appear in the oval opening behind the well. There are also a capillary tube (9) by which a fixed quantity of blood may be obtained; a medicine dropper (10), a candle (11), a black tube (12) to shut off the surrounding light from the eye.

We have, therefore: 1. A colored glass varying in tint with known quantities of hemoglobin. 2. A well divided into two equal parts and of known depth. 3. A capillary tube of known capacity.

The instrument is used as follows:

Puncture is made in the usual way and the tip of the capillary tube touched to the drop, as seen in the illustration (Fig. 784). No air space must occur in the tube. If the drop at first taken is not

Fig. 786.—Making Observation of Percentage of Hemoglobin with von Fleischl's Instrument. (Dark room.)

enough to fill the tube, in adding more, care should be exercised that the blood is flush with the end of the tube before again touching it to the blood drop. By gently tapping the tube this can be accomplished.

When the tube is quite full we *at once* insert the end into one of the subdivisions of the well, and with the medicine dropper send a stream of clear water forcibly through the tube (Fig. 785). This must be done promptly or the blood will clot in the capillary. The dropper need not be fitted on to the capillary tube, a procedure which often causes the latter to break. If the stream of water has been sent through with sufficient force the capillary will be entirely freed from blood. We then fill the well by dropping water with the dropper through the capillary. This fills the well and at the same time makes sure that all the blood has been washed through.

When the water has reached the top of the well a meniscus, which cannot be avoided, will be observed. When, however, we fill the opposite well with clear water, which we shall proceed to do directly, we must see that the meniscus in each well is of the same depth.

If the well should be full before all the blood has been washed from the capillary tube, then the dropper emptied of the water may be filled with the diluted blood already in the well and this passed through the capillary tube again until the latter is free of all trace of blood. Then the capillary tube in immersed into the well and the contents of the well stirred.

The other subdivision of the well is now filled with clear water, care being taken not to allow the contents of the two wells to mix over the division wall; also that the meniscus in each is of the same depth, as already mentioned.

Attention is called to the fact that the upper portion of the well unscrews for the purpose of cleaning the glass window at the bottom. These two portions should be tightly screwed together before using, so that the fluids will not mingle at the bottom of the well. Moreover, though the wells are the same in all instruments, the prisms of glass

vary one from the other in intensity of color. It is necessary, therefore, for the maker to test each prism and ascertain *what is the amount of normal blood* which will correspond to the color opposite the 100 mark. This amount is fixed by the capacity of the capillary tubes. Hence it follows that *the capillary tubes tested for a certain instrument should be used with that instrument only.* To insure this, *the number upon the handle of the capillary tube should be observed, to see that it corresponds with the number on the screw of the stand,* just behind the round opening for the well. Then, again, *the prism of glass must correspond with the stand,* and this is insured by seeing *that the number on the stand* and *that on the metal frame of the glass prism are the same.*

The above is a most clumsy method of numbering, arising probably from the fact that different workmen make different parts of the same instrument. The point to be borne in mind is that *the glass prism and the capillary tube must correspond,* and this can be made certain only by observing the above unnecessarily complicated system of numbering. *The wells are of the same depth in all instruments.* The figures on the handle of the capillary tube refer to the capacity of the tube.

We have now filled the two divisions of the well, the one with clear water, the other with a fixed quantity of blood and water.

The frame with the glass prism is now put in place, and the well over the prism, so that the prism shall be opposite that division which contains the clear water.

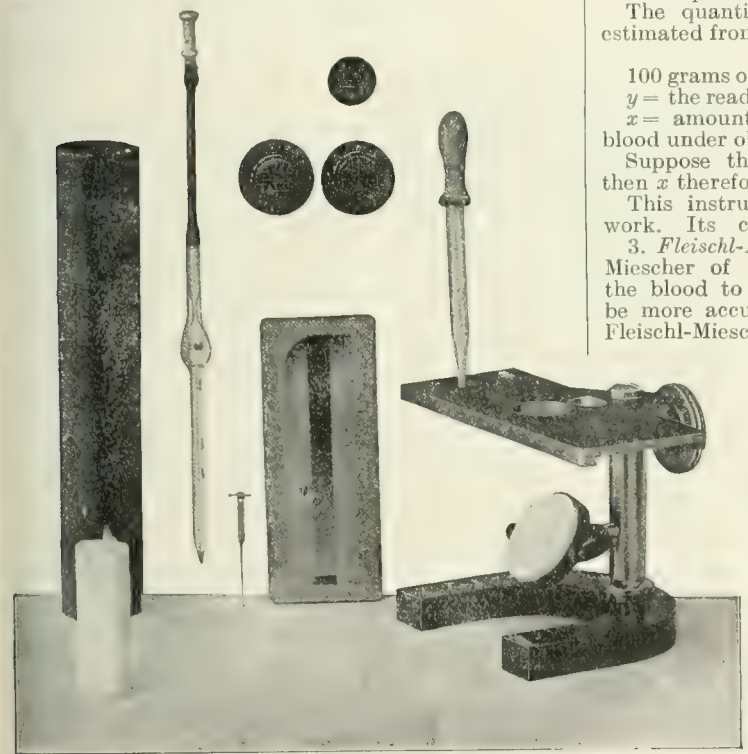


Fig. 787.—Von Fleischl-Miescher Hemoglobinometer.

We now transfer our operations to a dark room lighted only by a small candle. The instrument is placed about *eighteen inches away* from the candle, and a dark tube is placed over the well in order to shut off the surrounding light from the eye. The plaster-of-Paris reflector is adjusted so as to throw the light into the well, and then the screw of the glass prism frame is turned until the color of the diluted blood and that of the colored glass correspond (see Fig. 786). The figure which appears in the oval opening is now read, and this is taken

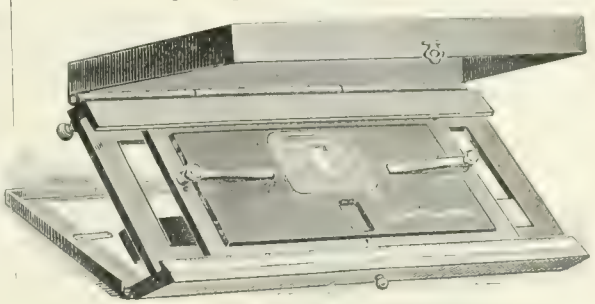


Fig. 788.—Taylor's Hemoglobinometer.

as the percentage of hemoglobin in the blood under observation. Some observers claim that there is a difference of several degrees between observations made with the operator in the position as shown in Fig. 786, and when he in to one side of the instrument. This claim, based upon difference in color appreciation of the eye in the two positions, seems a trivial one, and has not been borne out by the experiments of the writer.

As observers differ so greatly with one another in the comparison of colors, it is better to report a percentage of hemoglobin over a range of 5; for example, 65 to 70 per cent., 80 to 85 per cent., etc.

The quantity of hemoglobin in grams may be estimated from this by the following simple equation:

$$100 : 14 :: y : x$$

100 grams of blood contain 14 grams of hemoglobin.

$y =$ the reading on the von Fleischl scale.

$x =$ amount in grams of hemoglobin in 100 of the blood under observation.

Suppose the reading $100 : 14 :: 50 : x$ to be 50, then x therefore equals 7 grams of hemoglobin.

This instrument is very convenient for bedside work. Its chief objection is its expensiveness.

3. *Fleischl-Miescher Hemoglobinometer.*—Professor Miescher of Basel has devised a means by which the blood to be used in Fleischl's instrument may be more accurately diluted. The parts of the von Fleischl-Miescher instrument are shown in the illustration (Fig 787). The principal changes are, that instead of the capillary tube a graduated pipette is used, by means of which very accurate quantities of blood with accurate dilution may be obtained, and that wells of different depths are employed. There are a few minor changes also. We have been unable to discover any superiority in this instrument over the ordinary von Fleischl apparatus.

If the precautions already laid down by us in speaking of the von Fleischl apparatus are observed (*i.e.* to see that all the parts correspond), the instrument will be found quite reliable. Certainly we deprecate anything which increases the cost of the already too expensive von Fleischl instrument.

4. *Taylor's Hemoglobinometer.*—The following description and cut (Fig. 788) are from the advertisement of this instrument. I have had no experience with Taylor's hemoglobinometer. The price is $30.

"This apparatus was suggested . . . by Prof. A. E. Taylor formerly of the William Pepper Clinical Laboratory of the University of Pennsylvania Hospital. It consists of a fine capillary tube and mixing bulb with

Fig. 789.—Oliver's Hemoglobinometer. 1, Series of tinted glasses; 2, glasses with more delicate variation in tint to be used as rider; 3, well for reception and dilution of blood; 4, capillary tube for taking blood; 5, dropper; 6, candle and stand; 7, collapsible dark tubes.

bead, similar to that supplied with the Zeiss hemacytometer, a glass wedge of gradually increasing depth of color (the same as is used with the von Fleischl hemometer), and a rectangular glass plate with a square raised platform in the center. This raised platform, which is cemented to the plate nearer to one side, has in its center a circular cavity or cell of exactly one millimeter in depth. The rectangular plate is accurately fitted in a metal frame sliding in grooves, so that the cavity with its contents can be brought successively to any part of the wedge for color comparison.

"To use the apparatus a drop of blood is carefully drawn into the mixing tube up to the engraved mark, and distilled water is then drawn up till the bulb is entirely filled to the second engraved mark on the upper constricted end; the diluted blood is then mixed (by means of the contained bead) by shaking the bulb. The portion remaining in the capillary tube is then blown out and discarded. A part of the diluted blood is then blown out into the cavity in the platform of the rectangular plate until it is filled. A ground and polished square cover-glass is placed on top and the contents of cell are compared with successive parts of the wedge by reflected light from the white background until the color, as seen through both narrow rectangular diaphragms, agrees in depth, when the percentage of hemoglobin is indicated on the scale. . . .

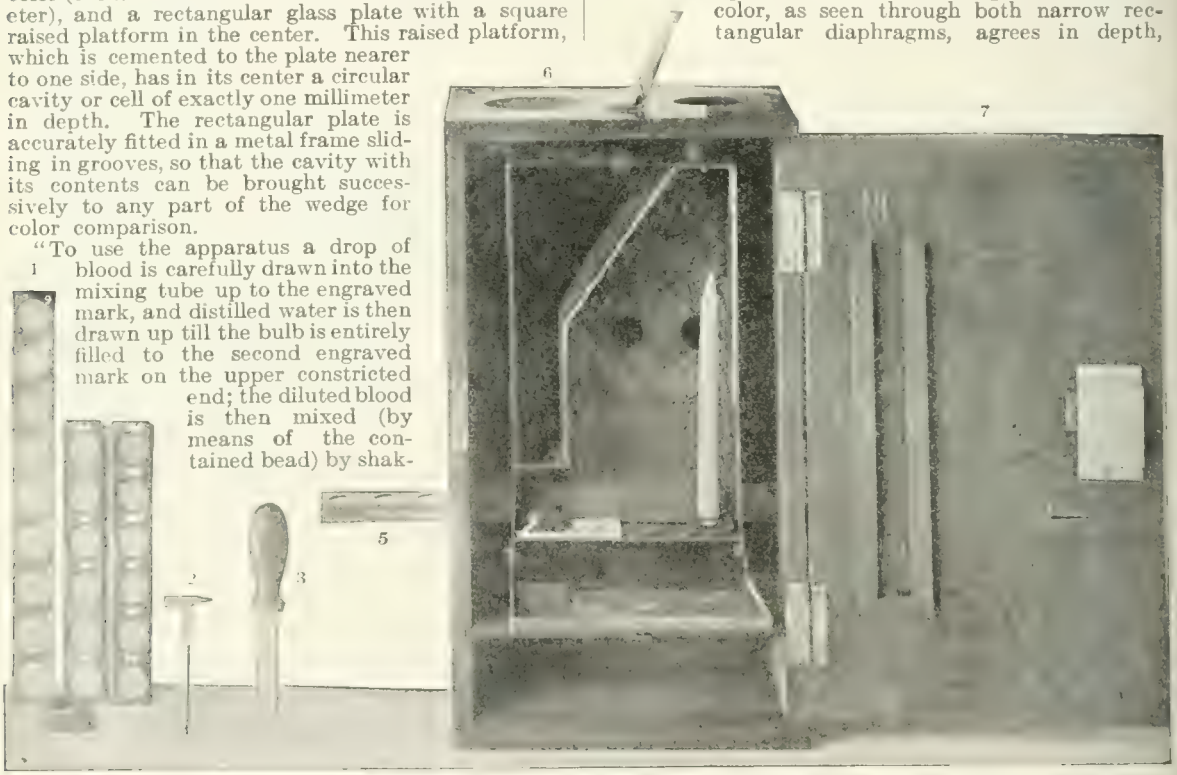


Fig. 790.—Dark Box for Estimating Percentage of Hemoglobin by the Tintometric Method. 1, Series of tinted glasses; 2, capillary tube for blood; 3, dropper; 4, well for diluted blood; 5, tinted glasses in position to one side of 4, in position, both of which can be seen and compared by looking through 6 when the door 7 is closed and the candle is lighted.

"The blood examined is of *a known accurate* dilution made with a pipette, which is very much greater in length than that employed in the von Fleischl

instrument, so there is less risk of inaccuracy. The quantity of the diluted blood to be compared with the Reichert wedge is *constantly* and *accurately fixed* by the use of a cell of one millimeter depth, somewhat similar to the cell employed in the Thoma hemacytometer. . . . The instrument can be closed and easily carried in the pocket, being about the same size as the case of the smaller Thoma hemacytometer.

"The capillary pipette supplied allows of a dilution of one to ten or one to twenty."

5. *Oliver's Hemoglobinometer.*—Dr. George Oliver of London at the same time that he devised his hemocytometer constructed a hemoglobinometer upon the principle of the tintometer of commerce.

As stated in describing the hemocytometer, the term tintometer is wrongly applied to the corpuscle-counting instrument. The hemoglobinometer of Oliver, however, does depend for its principle upon the comparison of tints, and it may therefore be called a tintometer.

The principle on which the instrument is based, namely, that every colored liquid, upon dilution or concentration, has a distinctive color curve (the same being true of colored glass) as characteristic as the specific heat of a substance, places this instrument in point of accuracy above that of Gowers, in which picrocarmine is used, and above that of von Fleischl, in which a gradation of colors is employed.

In Gowers' instrument, while the standard is fixed, yet the blood is continually changing in degree of dilution, and consequently the true color curve is destroyed. Moreover, as already stated, the standard picrocarmine changes color with age. In von Fleischl's instrument the dilution is fixed, but there is no uniformity of color in the area under observation. In Oliver's instrument there is a fixed dilution of a fixed quantity of blood compared with a fixed tint. The diluted blood and the glass that is compared with it must therefore have the same color curve.

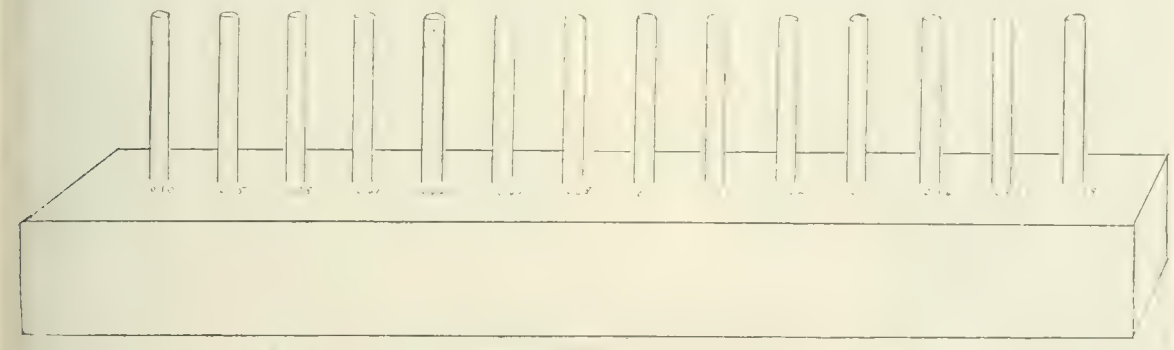


Fig. 791.—Roy's Specific-gravity Method. (Drawn by Dr. E. Dunning.)

The instrument consists of: twelve tinted glasses, in two sets of six each, mounted on white backgrounds of calcium sulphate* and ranging from 10 to 120; a capillary tube (five centimeters capacity) similar to but larger than that employed in the von Fleischl instrument; a dropper; a well with a white background of calcium sulphate; a thick cover slip (Fig. 789).

To use the instrument: Puncture is made in the usual way and the blood (quite a large drop) allowed to pass into the capillary tube, care being taken that no air spaces are formed; excess of blood is wiped away. The blood in the tube is then washed into the well by means of a stream of water applied with the dropper. As stated in describing the hemocytometer of von Fleischl, it is unnecessary and awkward to attach the rubber tube to the capillary. The well is filled to the top, the blood and water thoroughly stirred, and the blue cover-glass adjusted. A good light—preferably daylight—is obtained, and the eye screened as with the von Fleischl instrument; but the dark tube is to be held *about eight inches away* from the well, instead of upon it, as is done in using the last-named instrument. An expensive and, it would seem, unnecessary tube, called a camera tube, is supplied with the instrument.

In order to detect differences between 10 and 20, 20 and 30, etc., it is necessary to use riders each of which is equal to one degree.

By superimposing these riders until the exact shade of color is reached, and by then adding the number of riders employed to the next lowest figure on the scale, the percentage of hemoglobin is ascertained. For example, 40 + 3 riders = 43 per cent. of hemoglobin.

A candle flame may also be used for these observations; the illustration (Fig. 790) shows a box for making observations by candle flame. If such a box is not made use of, the candle should be placed about three inches from the point of observation.

The instrument has the disadvantage of being very expensive. It may be had of I. H. Smith and Co., Zürich, and of Tintometer Co., 6 Farrington Avenue, London, E. C., price, about $30.

6. *Tallqvist*[9] *Hemoglobinometer.*—Dr. T. W. Tallqvist, of the Medical Clinic of the University of Helsingfors, Finland, devised a method for quick estimation of the amount of hemoglobin by color comparison. The blood under examination, received upon a piece of special filter paper which is supplied with the booklet comprising the outfit, is compared by daylight with a carefully prepared table of colors representing known percentages of hemoglobin.

When the blood is spread on the filter paper a slight glaze is seen on the surface. Comparison must not be made till this has disappeared, which takes place in a minute or so.

This method is suitable for routine work only. Any variation from normal found with this method should be corroborated with the more accurate instruments. To the practitioner and dispensary physician it is of great value, for the small book can be carried in the pocket like a thermometer or stethoscope.

By aid of the von Fleischl-Miescher hemoglobinometer Tallqvist has tested this method and finds ten per cent. the degree of error.

It must be remembered therefore that ten or fifteen per cent. error is too great for a method to serve for more than an indicator directing the physician to make more accurate tests if any marked variation from normal be found.

7. *Dare's*[9a] *Hemoglobinometer.*—Dr. Arthur Dare of Philadelphia devised an instrument for estimating

* This, of many substances tested, was found by Oliver to produce the least confusing influence upon the appreciation by the eye of different tints.

hemoglobin without dilution of the blood. The instrument is somewhat on the plan of the Henocque hematoscope, but is much simpler and cheaper.

It is not however a cheap instrument and its structures are rather delicate for the rough treatment of a clinical or ward laboratory. A distinct advantage is that a dark room is not required (observer need only face a dark background) and that it is accurate and that the test can be done in much less time than with any other instrument of equal accuracy.

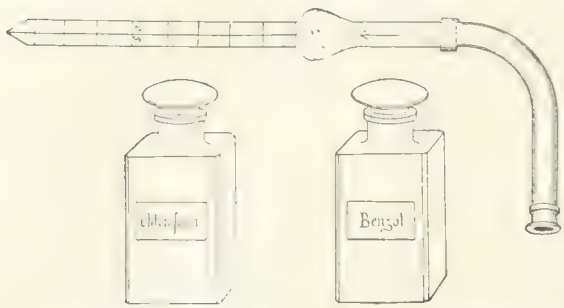


Fig. 792.—Reagents and Pipette Used in Hammerschlag's method. (Drawn by Dr. E. Dunning.)

8. *Sahli*[10] *Hemoglobinometer* (Hemometer).—This instrument is a modification of Gowers' Hemoglobinometer. By referring to Fig. 782, which represents the Gowers apparatus, Sahli's instrument will be understood if the following modification is added:

1. The two tubes instead of standing in a block are placed side by side in a block frame with a ground-glass background. These changes enable the reading to be made more readily.

Fig. 793.—Specific-gravity Method for Estimating Percentage of Hemoglobin. Blowing drop of blood from capillary tube into receiver containing benzol and chloroform.

2. The standard solution for comparison, instead of being picrocarmine which, as stated above, changes color in time, is a one-per-cent. solution of acid hematin which remains constant in color and does not decompose. This standard, as in Gowers, is contained in the sealed tube.

3. One-tenth normal solution of hydrochloric acid (15 c.c. of pure HCl to 1 liter of H_2O to which a little chloroform is added as a preservative makes such a solution which may be made up in quantity) is placed in the graduated tube up to the ten per cent. mark.

4. The blood is obtained with the pipette as with the Gowers instrument and added to the hydrochloric acid solution in the graduated tube. The acid acts upon the hemoglobin, changing it in a few minutes to acid hematin, which is the same substance as the standard solution contained in the sealed tube. We are thus comparing like solutions and this makes it possible to make our observation in any light desired.

5. The observation is now made by adding distilled water with a dropper till the colors correspond, when the percentage is read on the scale.

In the use of any of these color comparison methods the following points should be remembered:

1. Instruments inferior in workmanship and accuracy of standard are not uncommon. Each instrument should therefore be tested with others of known accuracy before admitting it to the stock of the laboratory.

2. Individuals may be defective in color detection and even individuals with no such defect may differ much in opinion on the same blood at the same time.

3. The eye after making many close observations may lose through fatigue accuracy of comparison.

C. *Specific Gravity Methods.*—It having been shown (by Siegel and Schmaltz) that the specific gravity of blood varies with the amount of hemoglobin contained, these methods of estimating hemoglobin have been placed among the important clinical tests.

Fig. 794.—Specific-gravity Method for Estimating Hemoglobin. Drop of blood suspended in the fluid (chloroform and benzol).

A number of methods have been devised, the most important of which are those of Roy and Hammerschlag. These two methods have for their principle the comparison of blood with heavier and lighter fluids of known specific gravity and such as are non-miscible with blood.

Roy, in his method, employs glycerin and water, fluids of widely different specific gravity. A series of test-tubes, as shown in Fig. 791, four centimeters in diameter and having a capacity of from 80 to 100 c.c., are filled with the two fluids, and the specific gravity of each is determined and marked. Blood is obtained in a pipette or capillary by the usual way. A drop is blown into each test-tube, *after the pipette has been submerged in the liquid*, and when that tube is reached in which the blood neither floats on the surface nor sinks to the bottom, the specific gravity of the liquid contained in that tube is read off.

Hammerschlag's method, which is clinically the more applicable, makes use of only one tube. In this method benzol and chloroform (Fig. 792) are the liquids employed, which, as before stated, differ widely in specific gravity and are freely miscible. The blood is introduced as in Roy's method, and the chloroform or the benzol is added until the blood floats in the mixture. The specific gravity of the mixture is then ascertained, which will also be that of the drop of blood.

Dr. Scott, who assisted me in the Cornell Clinical Laboratory, made the following comparative observations on the different methods of hemoglobin estimation:

Comparison between the Gowers and von Fleischl Instruments and the Specific-Gravity Methods for Hemoglobin Estimation.—In the accompanying tables von Fleischl's and Gowers' instruments and Hammerschlag's specific-gravity method were used. In these experiments the utmost care was taken to fulfil every requirement in the technique of each method. As a description of von Fleischl's and Gowers' instruments, and of their methods of use, has been given in another part of this article, the specific-gravity method only as employed in making these comparative observations will be described here. We have adopted Hammerschlag's method, which is

a modification of Roy's, as being best suited for the general practitioner.

In this method two fluids are selected which are

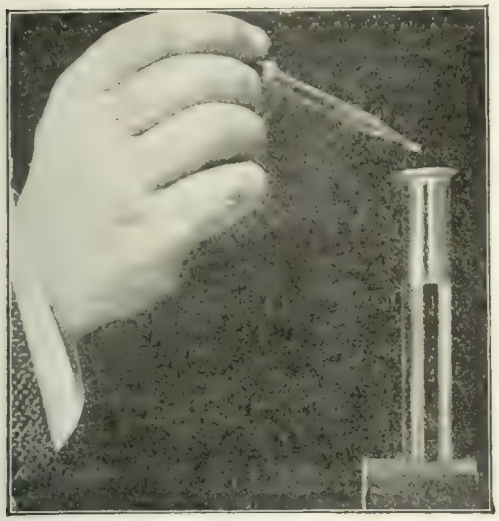


Fig. 795.—Specific-gravity Method for Estimation of Percentage of Hemoglobin. Adding fluids (benzol or chloroform) until drop of blood is suspended.

easily and readily miscible, and with neither of which will a drop of blood mix; further, the specific gravity of the one fluid is low, while that of the other is high.

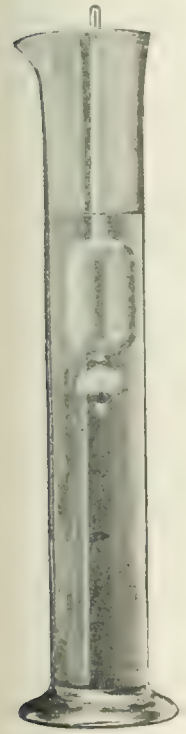


Fig. 796.—Specific-gravity Method for Estimating Percentage of Hemoglobin Taking specific gravity of fluid. Drop of blood seen suspended in fluid.

The fluids selected are benzol (sp. gr., 0.889) and chloroform (sp. gr., 1.526), which exactly fulfil these conditions. They have the further advantage of being cheap, and the whole apparatus required is likely to be found in every physician's office. We place some of the mixture (sp. gr., 1.050–1.060) in a dry clean cylinder, and carefully take a drop or two of blood in a Thoma-Zeiss mixer (any capillary pipette, however, will do); we then insert the end of the tube *just below the surface of the mixture*, and blow out a drop of the blood (Fig. 793). The blood is seen as a bright red globule which does not mix with the fluid, but either sinks to the bottom, floats on the top, or remains suspended in the fluid (Fig. 794). If it sinks to the bottom this is because it is heavier than the fluid, and more chloroform must be added. If it floats on the top, more benzol is required (Fig. 795). If it remains suspended, it is of the same specific gravity as the fluid (Fig. 796). It is well to add the necessary benzol or chloroform only one drop at a time from a medicine dropper (see Fig. 795), and to stir the fluid with a glass rod to cause complete mixture. It has been found that matters are very considerably simplified and much time and patience are saved, by having the mixture of such density that the drop of blood will sink to the bottom. It is much easier to make the globule rise by the addition of chloroform drop by drop than it is to cause it to sink by the gradual addition of benzol. Let the drop of blood remain suspended for a few minutes to see that it will neither float nor sink, and, then, when satisfied that it is stationary, ascertain the specific gravity by means of an ordinary hydrometer (see Fig. 796). By filtering the mixture of benzol and chloroform it can be used again and again.

The drop of blood will remain in the mixture for a considerable time without its specific gravity changing. In the illustration (Fig. 796) the drop remained suspended for forty-eight hours before the photograph was taken.

In Table I., below, a variation is to be noted between von Fleischl's and Gowers' estimates, but the variation is not constant in either direction. There is more steady agreement between those of von Fleischl and of Hammerschlag respectively; and this is more particularly seen in Table II., which gives comparative estimates of hemoglobin of the blood from each ear of the patient. Here, too, it will be seen that the specific-gravity readings are quite constant; while the von Fleischl readings vary somewhat, and those of Gowers vary considerably.

Dr. Scott's tables show very satisfactorily how little is the variation between the specific-gravity method, which is so simple in cost, and the expensive instruments. Even with the von Fleischl instrument one prefers to report his observations over a range of five points—seventy-five to eighty per cent., for example; while with the specific-gravity method the observations can be more precise—as in Dr. Scott's tables, where in most instances the observations are within a range of two or three points. Such reading would also include the reading with Gowers' or von Fleischl's instrument. It was for the purpose of determining the accuracy of the specific-gravity method that Dr. Scott made these observations, and our conclusion is that this method is, clinically, perfectly reliable and satisfactory.

Table I.

No.	Percentage of hemoglobin according to von Fleischl's hemoglobinometer.	Percentage of hemoglobin according to Gowers' hemoglobinometer.	Specific-gravity. Method of Hammerschlag.	Percentage of hemoglobin corresponding with this specific gravity.
1	68	69	1050	65
2	71	69	1052	68–9
3	68	67	1050	65
4	63	59	1049	60
5	75	69	1055	75
6	73	69	1054	72
7	78	71	1056	80
8	76	77	1054	72
9	78	77	1056	80
10	93	89	1059	91–2
11	81	81	1056	80
12	68	67	1052	68–9
13	73	69	1054	72
14	65	68	1051	67–8
15..	92	87	1059	91–2
16..	64	62	1050	65
17	91	92	1059	91–2
18..	53	57	1048	55
19.	82	88	1057	85
20..	61	55	1049	60
21....	52	49	1047	51–2
22	65	66	1050	65
23	78	76	1056	80
24....	81	73	1056	80
25	78	77	1057	85
26	77	73	1056	80
27.....	96	91	1060	95
28.....	62	69	1049	60
29..	85	66	1057	85

TABLE I. *Continued*

No.	Pertentage of hemoglobin according to von Fleischl's hemoglobinometer.	Percentage of hemoglobin according to Gower's hemoglobinometer.	Specific-gravity. Method of Hammerschlag.	Percentage of hemoglobin corresponding with this specific-gravity.
30.	58	57	1050	65
31.	71	69	1053	70
32.	68	68	1052	68–9
33.	86	79	1058	88–9
34.	82	83	1057	85
35.	81	83	1057	85
36.	78	73	1056	80
37.	80	74	1057	85
38.	80	78	1056	80
39.	87	83	1058	88–9
40.	90	90	1059	91–2
41.	75	72	1055	75
42.	68	67	1052	68–9
43.	81	83	1056	80
44.	81	84	1056	80
45.	75	76	1055	75
46.	88	88	1058	88–9
47.	86	83	1057	85
48.	78	72	1056	80
49.	85	87	1057	85
50.	82	80	1056	80

TABLE II

No.	Left ear.			Right ear.		
	Von Fleischl.	Gowers.	Specific gravity.	Von Fleischl.	Gowers.	Specific gravity.
1	87	83	1058	88	84	1058
2	90	90	1059	90	90	1059
3	75	72	1055	75	73	1055
4	68	67	1052	68	67	1052
5	81	83	1056	81	83	1056
6	81	84	1056	81	83	1056
7	78	76	1055	78	76	1055
8	88	88	1058	88	86	1058
9	86	83	1057	86	82	1057
10	78	72	1056	78	74	1055
11	85	87	1057	85	86	1057
12	82	80	1056	82	80	1056

4. COLOR INDEX.—This refers to the relation between the number of red cells and the percentage of hemoglobin.

Suppose the red blood corpuscle count to be 5,000,000; this being the normal, we may designate it as 100; then:

5,000,000 red blood corpuscles = 100
4,500,000 red blood corpuscles = 90
4,000,000 red blood corpuscles = 80
3,500,000 red blood corpuscles = 70
3,000,000 red blood corpuscles = 60, etc.

Suppose the hemoglobin to be 100 per cent. This is the normal. Then $\frac{100}{100}=1$, represents the normal state of the blood; 1 is the normal color index.

A general formula by which the color index may be arrived at would be the following:

$\frac{A}{B}$ = color index, in which A = percentage of hemoglobin and B the number of red blood corpuscles reduced to terms of 100.

Examples: Chlorosis, $\frac{50}{100}=0.5$ color index. Pernicious anemia, $\frac{40}{50}=0.8$ color index. Secondary anemia, $\frac{60}{80}=0.75$ color index.

Chlorosis, it will be seen, has the lowest index, pernicious anemia the highest; that is, in pernicious anemia each corpuscle is carrying more hemoglobin than is the case in chlorosis. This is the *value globulaire* of French writers.

5. VOLUME INDEX.—Capps[11] suggested this term to express the relation between the number of red cells and their volume. This is ascertained by using the hematocrit (see Figs. 768 and 769).

$$\frac{A}{B}=\text{volume index.}$$

A = bulk in percentage as seen on hematocrit tube.

B = number of red cells expressed in per cent. as in determining color index.

By comparing the color index and the volume index it is found that in pernicious anemia the color index is always less than the volume index which means that the high color index in this disease is attained not by excess of hemoglobin in the normocyte but by increase in size of the cell (macrocyte and gigantocyte) thus enabling it to carry more hemoglobin. In other anemias the volume index may be below the color index. Perhaps the most important observation in connection with this work is that rapid and acute dilution of the cell contents (probably) does not occur. Volume index has hardly received the attention that it deserves. More clinical observations are needed to confirm the value of this and as a sign in the early doubtful diagnostic stage of anemias.

IV. THE ANEMIAS DETECTED BY THE USE OF THE BLOOD-COUNTING AND HEMOGLOBIN-ESTIMATING APPARATUS.

(For complete table, see p. 197).

- Anemia
  - Primary
    - Chlorosis
    - Pernicious.
  - Secondary.
    - Hemorrhage.
      - Purpura,
      - Menorrhagia,
      - Hemorrhoids, etc.
    - Poisons.
      - Arsenic,
      - Lead,
      - Mercury,
      - Silver, etc.
    - Diseases...
      - Wasting diseases,
      - Malaria,
      - Inanition,
      - Tuberculosis,
      - Chronic suppuration,
      - Chronic Bright's,
      - Pyrexia, etc.

Terms. Oligemia—*ὀλίγος*, little, *αἷμα*, blood—too little blood. Oligocythemia—*ὀλίγος*, few, *κύτος*, cell, *αἷμα*, blood—too few blood cells. Oligochromemia—*ὀλίγος*, little, *χρῶμα*, coloring matter, *αἷμα*, blood—too little coloring matter. Leukemia—*λευκός*, white, *αἷμα*, blood—white blood. Leucocytosis—*λευκός*, white, *κύτος*, cell, *οσις*, full of—full of white corpuscles. The following terms are described in the text: Anisocytosis, poikilocytosis, lymphocytosis, eosinophilia.

V. STAINING OF DRIED SPECIMENS OF BLOOD.

Through the labors of Ehrlich we have learned that the blood corpuscles react variously to the aniline dyes: that some of the white corpuscles contain specific granules which in health react to these dyes in one way, while in disease these same granules react in a different way. So constant is this peculiarity that an entire system of diagnosis has become possible simply through the process of staining the blood.

As this branch of the study of the blood depends entirely upon the peculiar reaction, not of the corpuscles as a whole, but of certain parts of the corpuscles, our technique must be even more delicate than in any system of diagnosis already described.

1. Method Employed in Taking Dried Specimen of Blood.—There are two methods of preparing the blood for staining: (1) The slide method. (2) The cover-slip method.

(1) *The Slide Method.*—Puncture is made in the skin in the usual way. A drop of blood is received at one end of an absolutely clean glass slide. The edge of another glass slide is dipped into the drop of blood and drawn gently along the surface of the first slide. This produces a large and fairly thin smear of blood. The objections to this method are: (*a*) Too large a smear; (*b*) smear not thin enough; (*c*) unequally spread, thicker in one place than in another; (*d*) apt to mutilate the corpuscles. The cigarette-paper method has the same objections and gives the same unsatisfactory results (see also p. 160).

(2) *The Cover-slip Method.*—Several No. 1, seven-eighths inch, square Bausch and Lomb cover slips are *thoroughly* cleaned with alcohol and ether. Every trace of dust and cloudiness must be removed. These cover slips are placed on a sheet of white paper on a table near the patient. It is hardly necessary to state that they should be held *by the edges* and not by the flat surface—that portion which comes in contact with the blood, and which, therefore, we should take every precaution to keep clean. A lighted spirit lamp should also be at hand. The point of puncture is cleaned with alcohol and ether; this is more important in taking the dried specimen than in taking the fresh specimen. One of the cleaned cover slips is placed in the clamp forceps, as shown in Fig. 745, No. 4 *b*, and the forceps thus armed laid upon a table near at hand. Puncture is made in the usual way. After removing the first drop, the clamp forceps, holding the cover slip, is held in the left hand, and the second drop is received upon a cover slip held by the open forceps (see Fig. 745, No. 5) in the right hand. This is the first step, and is shown in Fig. 797.

The cover slip with the drop of blood is *immediately* transferred to the cover slip held in the clamp forceps, as follows: The edge of the cover slip upon which is the drop of blood and which is held in the open forceps is placed against the end of the limb of the clamp forceps holding the other cover slip. Thus held, the

Fig. 797.—Method of Taking Dried Specimen of Blood. First step.

cover slip is slowly lowered until the drop of blood almost touches the undermost cover slip. The right hand forceps is then opened and withdrawn, which allows the cover slips to come together with the blood between and spreading equally in all directions. This is the second step, and is shown in Fig. 798. If these steps have been carefully carried out, the blood specimen should appear as in the illustration (see Plate XIII., Fig. 1).

Directly the blood is no longer seen to spread the two slips are drawn apart, in such a manner, however, that they shall at all times be *parallel with each other.* This drawing apart must be *quickly done,* for if performed too slowly it will be found very difficult to

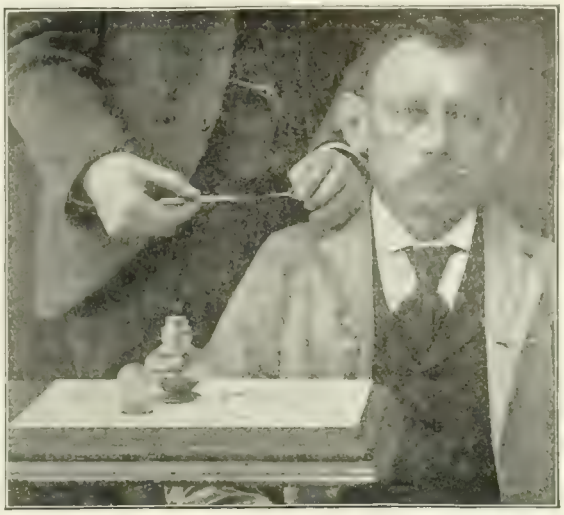


Fig. 798.—Method of Taking Dried Specimen of Blood. Second and third steps.

keep the slips parallel with each other—an essential point—otherwise the upper slip will be raised and make a clump of blood to form on the lower slip.

In order to act thus quickly, and to be sure of the slips coming away at one pull, it is well to take an additional hold upon the clamp forceps far down the limbs, near to the cover slip. This is the third step, and is shown in Fig. 798. The cover slips thus separated are now held from eighteen inches to two feet above the spirit lamp flame until the blood is quite dry. This is the fourth and last step, and is shown in Fig. 799.

It is recommended by some hematologists to use the thumb and forefinger in drawing the upper slip away, rather than to use the open forceps. When this plan is followed the corners of the cover slips should not exactly correspond, but one cover slip should be allowed to project beyond the other, so as to offer a margin to take hold of. As it is better not to touch the cover slip except with the forceps, and as the moisture of the skin readily adheres to the glass and ruins the blood specimen, the forceps method is preferable.

Thayer mentions that flies attack the dried specimens, eating holes in them. While this is undoubtedly true in some cases, yet the holes which one sees in dried specimens are more commonly caused by allowing the blood to dry in the air instead of using a spirit lamp. The writer has seen these holes in specimens taken in winter.

The prepared specimens may now be placed in a labelled pill box and kept indefinitely. The method of preparation here given permits of the preserving of specimens for a number of years, to be used for class purposes; or of sending them, packed in a little cotton, by mail to an expert. By learning this simple technique, therefore, a physician engaged in practice in a section of the country removed from laboratory opportunities, or one occupied in military duties, may take specimens and send them to a laboratory for examination.

The differential diagnosis of typhoid and malaria,

so important in military encampments, can thus be always aided by this simple technique. So recently as the Spanish-American war the neglect of this simple procedure led to most distressing cases of typhoid fever patients in delirium wandering about various cities. These cases had been discharged on sick leave with the diagnosis of malaria made on the fever and other general clinical symptoms. While at that time such negligence was open to severe criticism, to-day it would be unpardonable. Moreover, these patients were in many instances so indiscriminately overdosed with quinine that when ultimately seen at one of the city hospitals, the blood examination for malaria was greatly interfered with and certainly the typhoid victim gained little by this cinchonism.

Fig. 799.—Method of Taking Dried Specimen of Blood. Fourth step.

2. Method Employed in Fixing Dried Specimens of Blood.—Before proceeding to the work of staining it is necessary to "fix" the contents of the corpuscles so that they shall not be dissolved; and this is called fixation. The "living" blood will not stain because the corpuscles readily dissolve, giving up their hemoglobin even to water and all the corpuscular characteristics disappear. Smears may, however, be kept for a long time before fixing and staining. In most cases the stains act quite as well as when used soon after taking the specimen. An exception to this is in the Jenner stain which is more satisfactory if used on the recently taken specimen. A number of methods have been employed, which may be divided into fixation (1) by heat; (2) by fluids; (3) by vapors.

(1) *Fixation by Heat.*—(*a*) Ehrlich's copper-bar method (1878). A spear point made of copper and about eighteen inches in length is placed upon a support, as shown in cut (Fig. 800). A Bunsen burner is so located that the flame will strike the extreme point of the bar. The flame of an ordinary Bunsen burner, if applied to the extreme tip of a bar of this size, will be able to heat only a certain amount of the bar to a certain degree of heat; beyond which the temperature will not rise, no matter how long the bar is subjected to the flame. In other words, the flame has a limited heating power. This would at once be appreciated if we should attempt to heat, with the ordinary Bunsen burner, a copper bar five or ten feet long. We should not be surprised to find the far end of the bar cold, no matter how long the copper may have been subjected to the flame. We should realize that the little flame, with its limited heating power, could not heat so large a bar. The heating power of an ordinary Bunsen burner does not extend, on a metal bar, beyond the distance of eighteen inches. What we wish to obtain by this heating procedure is the fixed boiling line on the bar. This we accomplish by placing drops of water upon the surface of the bar, about twenty minutes after it has been subjected to the flame; and directly the point farthest from the apex of the bar at which a drop of water boils away is found, we draw a chalk line across the bar at that point. This marks the temporary boiling line. After the lapse of a few minutes we put another drop of water just beyond the line; if the boiling point has extended the drop will boil away, and we then draw a second line at the new point and still farther from the apex. This procedure is repeated until a point is reached at which the water does not boil away, when we know that the limit of the heating power of the flame has been located. Once the permanent boiling line is thus located, no matter how long the flame is allowed to attack the apex of the bar, the line will never extend any farther from the apex. The confirmation of the fact that this line has been reached is afforded when a drop of water boils away almost at once on the flame side of the line, but remains until slowly dried off on that side of the line away from the flame. This, then,

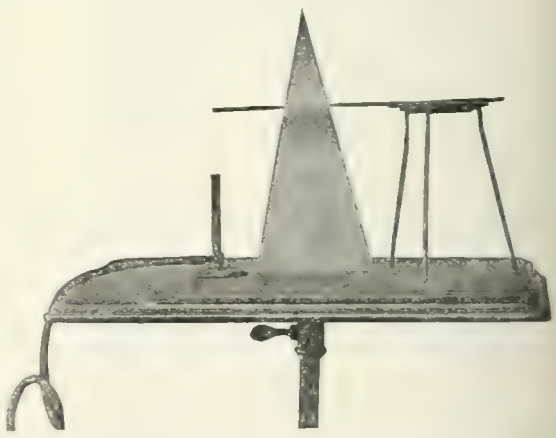


Fig. 800.—Ehrlich's Copper-bar Method of Fixation of Blood Specimens by Heat. 1, Bar placed in upright position to show shape; 2, bar in place with Bunsen burner at tip.

is the line we seek, and it is called the fixed boiling point or line. To fix blood by heat the specimen must be subjected to a temperature above 110° C. and below 140° C. By the procedure just described such a temperature zone is determined. The blood specimens, as above prepared, are now laid *blood side*

up either upon this line or directly to the boiling side of it. If the boiling line has been accurately located, it is, in the writer's experience, rather severe treatment to place the specimens blood side down on this line, as recommended by Cabot.[12] Specimens so placed are allowed to remain from forty minutes to an hour, except in cases of pernicious anemia or of grave secondary anemia, when a much shorter time—perhaps only twenty minutes—is sufficient. This is not satisfactory for malaria specimens. One should be careful not to allow draughts to influence the direction of the flame, as in this way the bar is chilled and the boiling point thereby altered for a period of several minutes. Ehrlich's copper-bar method is a good one, in the thoroughly equipped laboratory, for specimens prepared for class purposes; but it is tedious and calls for much watching, and has been replaced by quicker and simpler methods which seem, so far as one can at present judge, equally good.

The heat method would seem to render stains *more permanent* than when fixation is accomplished by other agents. I have specimens fixed by heat and stained fifteen years ago which still retain the brilliancy of the dyes, while those treated by the other fixation methods at a much later date have faded. For valuable specimens this is of decided importance. Specimens from cases of extreme anemia, however, must be heated with great care. They are readily destroyed by overheating.

(*b*) A quick heat method, and one applicable to office work, is that by means of the spirit lamp. The specimens, taken as above described, are simply held about two feet above the flame until the blood is thoroughly dried; or the cover slips may be heated to 60° or 70° C. (a temperature which can be borne by the skin) before taking specimens. This serves for immediate staining and examination; but for specimens which are to be kept for a long time, or in which accurate differential examination is desired, it will be found unsatisfactory.

(*c*) Another fairly quick heat method is that by means of the thermostat, brought gradually to a temperature of 150° C. and kept at this degree of heat for from forty minutes to an hour. This is as satisfactory as the copper-bar method, but not as readily carried out.

(*d*) Another simple means is to make use of the top of a steam register, upon which the specimens are allowed to remain for from forty minutes to an hour. This is a very good and convenient method. Care must be taken that no moisture shall be on the metal.

(2) *Fixation by Fluids.*—(*a*) Of these, Nikiforov's method is the best. It calls for equal parts of absolute alcohol and ether. The specimens are immersed in this liquid for from two to four hours. This, next to the formalin method given below, is the best for malarial specimens. For quick work fairly good results may be obtained from an immersion lasting twenty minutes.

(*b*) Dr. G. A. Tuttle devised a method which is described by Dr. Fred P. Solley, in the reports of the Pathological Department of the Presbyterian Hospital, New York City. The following is taken from those reports:

"Experiments were made by Dr. G. A. Tuttle with chromic acid, and after trials of different strengths for varying periods of time he found that a two-per-cent. solution poured on the film and allowed to remain for exactly thirty seconds gave uniformly good results, both red and white cells taking up their special stains clearly and surely. The nuclei and granules of the leucocytes stain quite as sharply as in the best specimens fixed by heat—while the protoplasm of the mononuclear lymphocytes is usually better stained than by the latter method.

"By this method, then, the whole process of preparing the specimens for examination is reduced to five or six minutes, and when the films are evenly and thinly spread the preparations are certain to be available for accurate differential computation. The red cells occasionally show defects as a result of the action of the acid; but this usually means that the solution has been left on too long, or that the films were unevenly spread. Indeed, the spreading of the films is of the utmost importance in securing satisfactory results by any method. . . . The two-per-cent. chromic acid solution is spread from a dropper over the film, the cover glass being held in a staining forceps. After thirty seconds the acid is thoroughly washed off and the excess of water removed by tapping a corner of the square on filter paper. The stain is then poured over the film in the same manner, and washed off quickly after three minutes. The specimen may then be dried between layers of filter paper and is ready to be mounted in balsam.

"By employing this method a complete blood examination may be carried out in a little over an hour at the bedside of the patient, often affording valuable information in cases in which the desirability of surgical intervention is in question."

This method has proved most satisfactory in my hands.

(*c*) Bichloride of mercury and Müller's fluid (formula, see p. 170, footnote) may be used, but the results are uncertain.

(*d*) Formalin method. Five drops of ten-per-cent. formalin solution are mixed with 10 c.c. of 95 per cent. alcohol. The cover slips are immersed in this for thirty seconds.

Futcher and Lazear reported this as a most satisfactory method for malarial blood. The writer has found that when using the Ehrlich eosin hematoxylon stain this is a thoroughly reliable fixing method. The statement of Futcher and Lazear as to its value for malarial specimens is, in the writer's opinion, to be indorsed.

(3) *Fixation by Vapors.*—In this method cotton soaked in two-per-cent. formalin is kept at the bottom of a wide-mouthed bottle. The specimens are subjected to the vapor from this, with the cork in the bottle, for from fifteen to thirty seconds. This is a good office-table and classroom method. During one winter the students in their laboratory and bedside work at the Cornell University Medical College prepared all their blood specimens by this method. While quickly obtained, the stains were not permanent, so that in a few months they had almost wholly faded out.

(4) *Fixation by Fixing Agent in Stain.*—This method has become the popular one because the fixing and staining are accomplished in one step and in a few minutes. The stains must, however, be well prepared and the specimens must not be overstained. It is a more common error to over- than to understain. If there is uncertainty about the stains or if a hospital interne finds it difficult to get good results it is better to fix by heat or alcohol and stain with eosin and methylene blue. I have found that this simple method will bring good results in the laboratory of a general hospital in which men have been struggling unsuccessfully with the more complicated stains. In trained hands though there is no method more satisfactory than the fixing stain. These stains will be given under head of *Blood Dyes*.

3. Blood Dyes, their Source and Classification.—The following is not an exhaustive article upon blood staining; it treats of this subject only in so far as it is part of the apparatus used in the clinical examination of the blood. So much has lately been accomplished in the differential staining of the malarial parasite that this part of the subject of blood staining will be treated of under other heads (*Histological Technique, Malaria*, etc.).

In the process of distillation of coal gas from bitu-

minous coal, for ordinary lighting purposes, there condenses upon the pipes a "thick, black, opaque, viscid liquid" which is known as coal tar. From this coal tar, among the many other useful products (paraffin, naphtha, creosote, carbolic acid, pitch, etc.), has been separated benzol. When benzol is acted on by nitric acid, nitrobenzol is formed, and this, when treated with nascent hydrogen, produces aniline, which is an oily liquid, aniline oil occurring as a by-product of the process. This aniline is a chemical base and unites with acids to form salts. These salts are of a great variety of most beautiful colors—violet, green, purple, etc.—and are the origin of our valuable stains in microscopic work. Benzol being the source commonly employed in the preparation of the aniline dyes for commerce, this would make these dyes apparently by-products of coal tar. Aniline, however, is a direct product, but in too small quantities to make it profitable to separate it. The word anil comes from the name of a plant from which indigo is made; the word signifies purple, and is applied to this product of coal tar as purple is one of the most striking colors produced by the combination of aniline with an acid.

The stains used in microscopic work are manufactured by Grübler in Germany and sold in powder form. From these, various strengths of stain may be made. The system by which these powders are classified is at times confusing. It is to be regretted that the names are selected so as purposely to convey no information beyond that of enabling the compounder to refer to his records and there learn the secret process which produced the stain. So no further explanation can be given of this classification. Many of these names, as tropaeolin ōō and orange "G," were given by the commercial compounders and have been adopted by Grübler, who confines himself to the preparation of stains for scientific purposes. Eosin is from the Greek word meaning the dawn. Methyl blue and methylene blue differ the one from the other in that the former, mixed with sodium hydrate, changes color to a reddish brown, the latter to violet. Methyl blue is the stain usually employed in blood work.

The stains are grouped into two general classes—acid and basic. These terms do not indicate a litmus reaction, and are therefore not to be taken in the strict chemical sense. The stains are for the most part neutral salts, that is, made up of a base and an acid, but neither acid nor basic in reaction. Now if the acid part of a salt is the staining element in the salt, the stain is called an acid stain. Example: ammonium picrate, which is a salt made up of ammonia, *the base*, and picric acid, *the acid*. Picric acid is the element in the salt which stains; hence the name *acid stain*. Another stain is rosanilin acetate—rosanilin is *the base* and acetic acid is *the acid*. The base in this salt is the staining element, and hence the name *basic stain*. The term *neutral stain* refers rather to a peculiarity of the tissue than to the stain.

According to this grouping of the stains the tissues are also classified. Those tissues which stain with an acid stain only are called eosinophilic; those which stain with a basic stain only are called basophilic, and those requiring both an acid and a basic stain are called neutrophilic. Tissues which consistently stain with an acid stain were termed by Ehrlich eosinophilic, because eosin was the most striking stain of the acid group. Now that we have all our stains clearly classified, however, it is better to adopt a term referring to the entire group rather than to a single stain in the group. Oxyphilic (ὀξύς, acid; φιλέω, I like) is therefore a better word.

4. Tissue Affinities for Dyes and their Classification.—The following list contains only a few of the more common stains.

Acid.	Basic
Eosin,	Rosanilin acetate,
Fuchsin (acid),	Fuchsin (basic),
Orange "G,"	Saffranin,
Picric acid,	Methyl blue,
Aurantia,	Methyl violet,
Indulin,	Methyl green, etc.
Nigrosin,	
Tropaeolin ōō, etc.	

The *Tissues*, according to the explanation just given, are grouped by Ehrlich as follows:

1. Oxyphilic (ὀξύς, acid; φιλέω, I like), synonymous with eosinophilic (acidophilic is a hybrid, and should therefore be discarded), refers to tissues taking only acid stains. The Greek letter α is used to designate oxyphilic granules. Example: eosinophiles of human blood.

2. Amphophilic (ἄμφω, both)—refers to those tissues staining equally well with either an acid or a basic stain. Example: the bone marrow of rabbits. There are no amphiphilic granules in human blood. The Greek letter β is used to designate amphophilic granules.

3. Basophilic refers to tissues taking only basic stains. Example: Mast cells. The Greek letter γ is used to designate basophilic granules.

4. Neutrophilic refers to tissues requiring both an acid and a basic stain. Example: polynuclear leucocytes. The Greek letter ϵ is used to designate neutrophilic granules. (The word neutrophilic is a hybrid—*neutrum*, neither, and φιλέω, I like. Oudeterophilic (οὐδέτερος, neither), would be more correct but not as simple, perhaps, as the present word.)

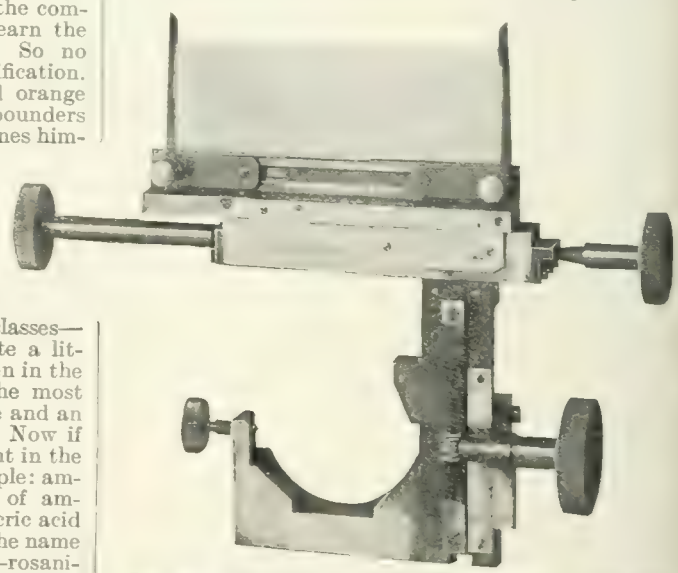


Fig. 801.—Mechanical Stage. 1, Slide in place; 2, space and screw for reception of and fastening to upright of microscope; 3, screw for lateral motion of slide; 4, screw for forward and back motion of slide.

In order to demonstrate these staining reactions of the various blood corpuscles and their granules, the stains should be each in turn applied to specimens of blood; then the specimens should be examined, and those parts which take the stain should be noted.

For example, subject a specimen of blood to an acid stain—eosin. Result: Red cells stained; eosinophile granules stained; granules of polynuclear leucocytes very faintly tinged; *all else unstained.*

Subject a specimen of blood to a basic stain—methyl blue. Result: Nuclei of all leucocytes stained; granules of polynuclear leucocytes very faintly tinged; *all else unstained.*

Subject a specimen of blood to a neutral stain – eosin and methyl blue. Result: Red cells stained red; eosinophile granules stained red; nuclei of leucocytes stained blue; granules of leucocytes stained reddish-blue.

The blood thus prepared is now examined and the percentage of normal cells, peculiarities of staining, and cells not normally in peripheral circulation are noted. In order to examine these fields accurately and not to recount the cells we employ the mechanical stage (Fig. 801). This is so constructed as to enable one to move the specimen a microscopic distance at a time from side to side, up and down, and across diagonally. It is moreover supplied with a register by means of which the observer may take note of his whereabouts in the field, so that having moved away from the field, he may return to it again by causing the figures upon the register to stand according to the position previously noted. In this way corpuscles may be restudied and at the same time the whole specimen thoroughly examined.

When the blood has been fixed as already described it is then subjected to the stains for varying lengths of time. The following are a few of the stains and formulæ employed in blood work:

5. Formule for Blood Stains.—1. *Eosin:* 0.5-per-cent. alcohol solution; one-half to one minute. Methyl blue—saturated aqueous solution; one-half to one minute.

2. *Ehrlich's triple stain:*

1	Acid fuchsin	3.5
	Water	2.0
2	Orange "G"	6.0
	Methyl green	6.5
	Water	10.0
	Absolute alcohol	5.0

The brackets show the order in which ingredients should be mixed in preparing the stain.

3. Carbol thionin.[13]—Saturated solution of thionin in fifty-per-cent. alcohol, 20; two-per-cent. carbolic acid, 100. (Should stand several weeks before being used.) Stain for from ten to fifteen seconds. Especially good for malarial parasite.

4. Eosin hematoxylon of Ehrlich.—Eosin (cryst.), 0.5; hematoxylon, 2; absolute alcohol, 100; distilled water, 100; glycerin, 100; acetic acid, 100; glacial acetic acid, 10; alum (in excess), 50. (Should be made several weeks before using.) Alum aids in dissolving hematoxylon.

5. *Jenner's.*[14]—A stain which also fixes the blood: (a) 1.2 per cent. watery sol. eosin (Grübler's sol. in water eosin). (b) 1 per cent. watery sol. methylene blue (Grübler's medicinal). Equal parts of a and b mixed, well stirred and allowed to stand from twenty-four to thirty-six hours. The eosin and methylene blue precipitate each other, throwing down a lustrous metallic precipitate. Filter off this precipitate and wash till only a faint blue tinge remains. Collect the precipitate and dry *without heat.* The powder so prepared may be kept till needed. To use: dissolve half a gram of the powder in 100 c.c. of *pure* methyl alcohol.

To stain: air-dried specimens are allowed to remain in this stain two or three minutes. The time must be determined by each worker for each stain. The stain is then *promptly* washed off till only a faint tint remains. This is certainly the most valuable stain, for general work, which so far has been devised. Many modifications of this stain have appeared.

6. *Nocht's.*[15]—For the chromatin of the malaria parasite this stain, which is a modification of that devised originally by Romanowski, has so completely taken its place that it is more profitable to refer to Nocht's modification directly. The specimen must be fixed in methyl alcohol.

The important ingredient in this stain is polychrome methylene blue which has been treated chemically so that when in combination with eosin it produces a dye which stains the malarial parasite a brilliant red.

To Prepare the Stain.—To 2 c.c. water add two or three drops of one-per-cent. aqueous solution of eosin. To this add the polychrome solution drop by drop until only a faint tint of the eosin remains. A precipitate immediately forms, and in order to prevent this from settling upon the specimen which should now be placed in the stain, *put the blood side of the specimen down.* Let it remain about five or ten minutes and then wash thoroughly.

Ewing[16] gives the most satisfactory directions for mixing the solutions and these will be found in the reference here given. The polychrome blue is produced by heating a one-per-cent. solution of methylene blue with 0.5 per cent. sodium carbonate for forty-eight hours at a temperature of 55° C.

7. *Goldhorn*[17] has also devised a modification of the Romanowski-Nocht Stain.

8. *Leishman Chromatin Stain.*[18]

9. *Wright's*[19] *Chromatin Stain.*

10. *Giemsa's*[20] *Methylene Azure Stain.*—This stain is the result of an effort to further simplify the Romanowski-Nocht stain by extracting the active staining agent in the polychrome blue. Wood[21] has made valuable additions to the technique of preparing and using this stain.

11. *Hastings*[22] working upon all the foregoing has devised a modification which is among the more important because of its general application to blood conditions and because of the accuracy and certainty with which it brings out the normal and pathological features of the corpuscles. In the article referred to these features are fully discussed and illustrated by two beautiful plates, one of which is here reproduced by permission of the author and of the publishers.

It is well to remember that in most instances each individual stain has its peculiarity with regard to intensity of staining depending upon the age of the stain, the character of the ingredients used, etc. The formulæ and directions given in any description should be taken as guides only and every stain should be tested out with regard to time, degree of washing, etc. In a hospital laboratory much time would be spared and many failures prevented if the directions for the use of each individual stain were placed on the label. At the same time it must be remembered that stains change their characteristics with age and that such directions must be changed accordingly.

12. *Müller's* fluid, see p. 170, footnote.

13. *Formalin* solution for fixing blood, see p. 189.

14. *Hayem's* solution, see p. 162.

15. *Pacini's* solution, see p. 162.

16. *Toison* solution, p. 165.

17. *Pratt's* solution for preserving the blood plates, p. 174.

Vital Staining.—The staining of the living (unfixed) blood has received considerable attention in recent years.

In Dr. Vogel's hands the most satisfactory dyes for vital staining are brilliant cresyl blue (Grübler) and polychrome methylene blue solution, put up by Grübler. There are several ways of making the preparations. Vogel recommends the following: A saturated alcoholic solution of the cresyl blue is smeared in a thin film on the slide. As the alcohol evaporates a delicate layer of the dye is left on the slide. On this the blood is smeared in the usual way, and as it dries the cells become stained.

Another method is to use a saturated solution of cresyl blue in salt solution with a little two per cent. sodium oxalate solution added, drawing a little blood into the capillary portion of a red cell mixer and following with the solution just mentioned. The mixture can then be centrifugalized and smears made from the sediment.

The polychrome methylene blue can be used in a

mixture containing equal parts of the solution as it is delivered by Grübler and physiological salt solution. To about 2 c.c. of this five drops of two per cent.

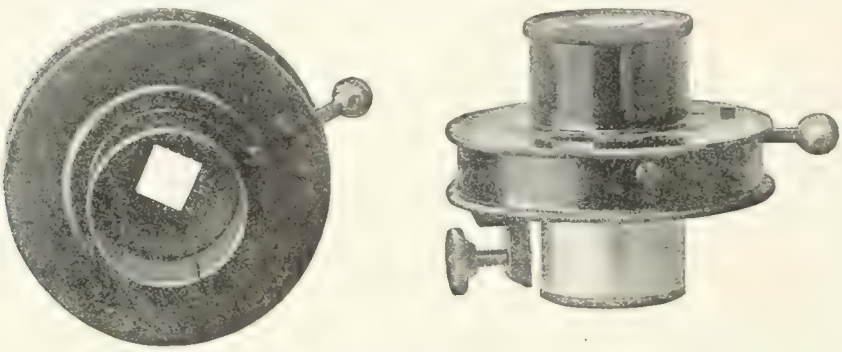


Fig. 802.—Ehrlich's Eyepiece for Determining the Relative Values of White and Red Cells in a Dried Specimen of Blood. 1, Screw for fastening eyepiece to microscope; 2, handle by means of which the square aperture (3) may be altered in size; 3, aperture reducible to definite relative sizes by observing notches seen on upper margin of square.

oxalate solution may be added to prevent clotting. This stain can be used in a red cell mixer as just described. By doing the staining in the mixer, although it is a little more troublesome, one is less likely to get artefacts and the results are more convincing.

Neutral red has also been suggested for this purpose, but it is less satisfactory than the two dyes just mentioned. Methylene blue, methylene azure, and pyronin methyl green are also used.

6. Mechanical Eyepieces.—(*a*) *Ehrlich's Eyepiece* (Fig. 802) supplies an important need. This instrument is so devised that accurate fields may be measured off on the dried specimen of blood and the relative numerical values of white and red corpuscles thereby ascertained. The instrument is constructed like an eyepiece, and may be fastened to the microscope in place of the eyepiece. A handle projects from one side of the instrument, and when this is moved the square aperture noted on looking through the eyepiece is seen to increase and decrease equally on all sides according to the direction in which the handle is turned. On the uppermost side of the square (see Fig. 802) three notches will be noted.

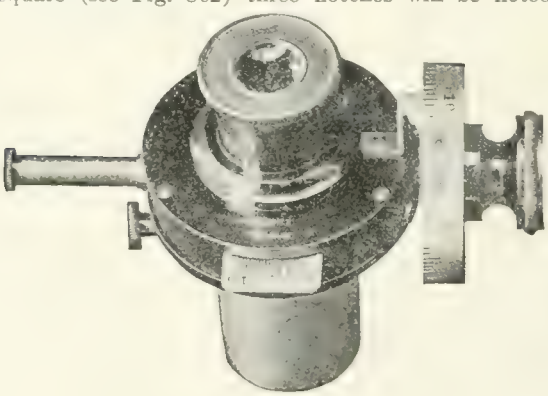


Fig. 803.—The Eyepiece Micrometer.

When the handle is placed so that the square is at its greatest size the dimensions of this square will be just sixteen times that of the square formed when the first notch is covered. The second notch indicates a square four times as large as when the first notch is covered; the third notch indicates a square nine times as large; and the largest square, as stated, is sixteen times as large as the smallest.

Thus by counting all the red cells in the first or smallest square of a number of fields, and all the white cells in the fourth or largest square (which is sixteen times as large as the smallest) of a number of fields, and multiplying the number of red cells by sixteen, we get the ratio of red to white cells in a dried specimen.

(*b*) *The Eyepiece Micrometer* (Fig. 803) is of so simple construction and mechanism that its employment is to be recommended for more accurate clinical reports on the size of the blood corpuscles.

The following explanation is taken from the Leitz advertisement of the instrument:

Micrometer Measurements.—The scale of the eyepiece micrometer is divided into $\frac{1}{10}$ millimeter. Each of these divisions represents, according to the objective used, a certain absolute linear measure of the object, as shown in the following table:

Number of objective.	Absolute length of object represented by one division of the eyepiece-micrometer scale. Millimeters.	Number of objective.	Absolute length of object represented by one division of the eyepiece-micrometer scale. Millimeters.
1	0.054	7	0.0026
2	.028	8	.0020
3	.015	9	.0017
4	.012	Immersion $\frac{1}{12}$	.0022
5	.0048	Immersion $\frac{1}{20}$	.0018
6	.0034	Immersion $\frac{1}{30}$	.0014

When making micrometer measurements it is absolutely necessary accurately to maintain the tube length at 170 millimeters. If this is neglected the measurements become unreliable or even worthless.

The above micrometer values are measured with eyepiece II.; in the other eyepieces they differ in an inappreciable degree.

Example: Let a scale of *Hipparchia janira*, as seen with objective 6, cover 54 divisions of the scale longitudinally and 20 division transversely. Its actual length will then be $54 \times 0.0034 = 0.184$ millimeter, and its breadth $20 \times 0.0034 = 0.068$ millimeter.

Suppose a valve of *Pleurosigma angulatum*, measured with objectives 4, 6, and 7, to cover 21, 74, and 98 divisions respectively; then the measurements of its length represent the following absolute dimensions:

Objective 4 : $21 \times 0.012 = 0.252$ millimeter.
Objective 6 : $74 \times 0.3004 = 0.252$ millimeter.
Objective 7 : $98 \times 0.0026 = 0.255$ millimeter.

Tables of Magnifications.—The image seen in the microscope produces upon the eye the same effect as an object seen at the normal distance of distinct vision, *i.e.* ten inches.

If, therefore, a rule be placed at the foot of the microscope at a distance of ten inches from the eye, it can be compared with the microscopical image of a scale divided into $\frac{1}{100}$ millimeter. The quotient is the magnification of the objective and the eyepiece combined.

If, *e.g.* ninety-two millimeters of the rule are found to cover $\frac{7}{10}$ of the image of the micrometer scale, it

EXPLANATION OF
PLATE XV.

EXPLANATION OF PLATE XV.

1–2, Polynuclear neutrophiles.
2a, Plates; 2b, False-plates.
3–4, Polynuclear eosinophiles.
5–9, Lymphocytes.
10–12, 14, 14a, 15, Large mononuclears.
14a, "Old, aged" lymphocyte of Michaelis and Wolff.
13, 13a, Stimulation forms of Türk.
16, 16a, 17, Transition-forms.
18–20, Myelocytes.
21, "Large lymphocyte" of acute lymphatic leukemia (Türk's lymphoid-marrow cell).
22, 22a, Mast-cells.
23, Normal red cell.
24, Normoblast with basic granules in protoplasm.
25, Megaloblast.
26, Granular basophilia in red cell.
27–30, Malaria parasites.
31, Stippling in red cell invaded by tertian parasite.

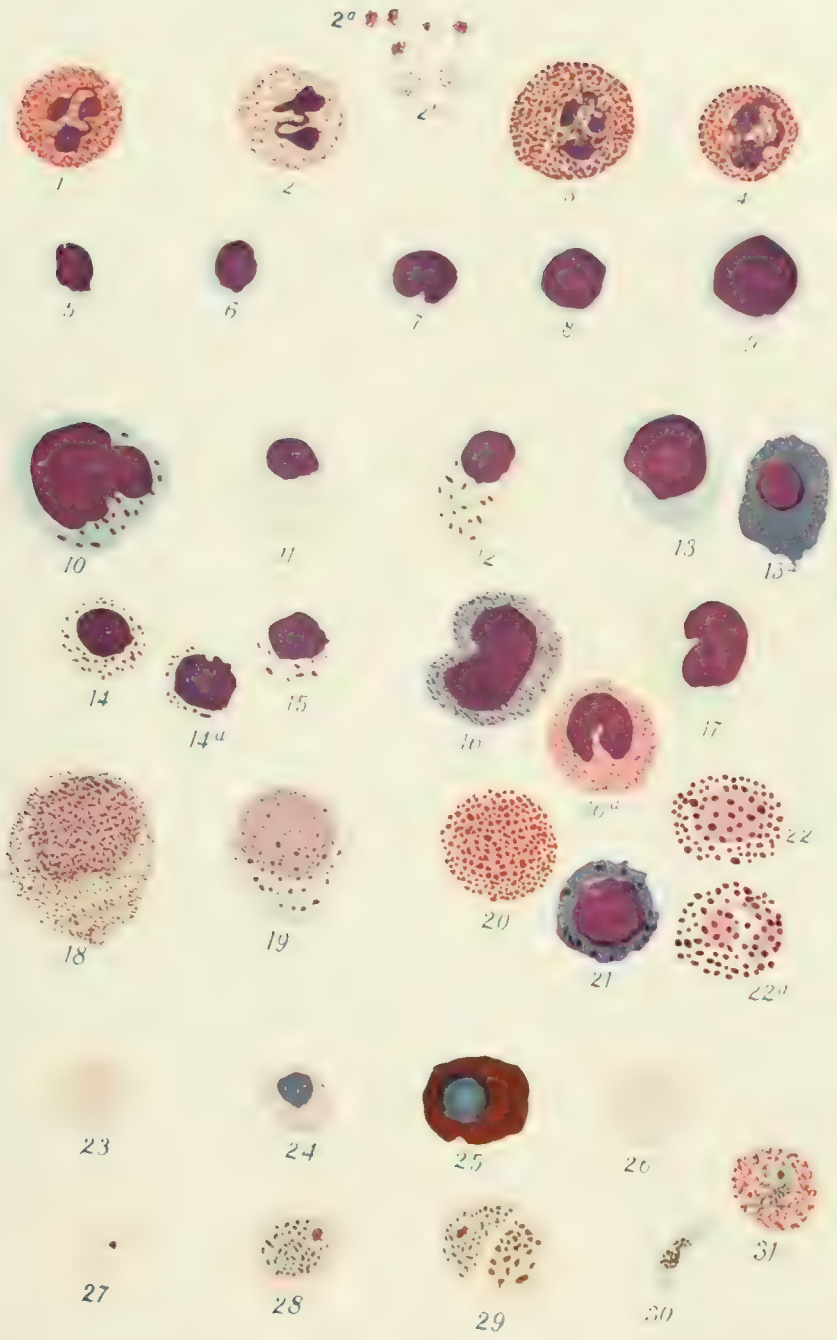
CLASSIFICATION OF WHITE CELLS SHOWN IN PLATE.

In normal blood:

Polynuclear neutrophiles	Figs. 1, 2.
Polynuclear eosinophiles	Figs. 3, 4.
Lymphocytes	Figs. 5, 9.
Small	Figs. 5, 7.
Large	Figs. 8, 9.
Large mononuclears	Figs. 10, 12, 14, 14a, 15.
Transitionals	Figs. 16, 16a, 17.
Mast-cells	Figs. 22, 22a.

In pathological blood:

Myelocytes	Figs. 18, 20.
Neutrophilic	Fig. 18.
Basophilic	Fig. 19.
Eosinophilic	Fig. 20.
Lymphoid-marrow cell	Fig. 21.
Stimulation forms	Figs. 13, 13a.



Showing the Results Obtained by Hastings' Modification of the Nocht-Jenner Stain.

T. W. Hastings, M. D., *Journal* [illegible] *Medicine*, June 10, 1905.

ollows that the magnification is $\frac{2}{3}\frac{2}{0}=130$. The ables of magnification have been compiled in this manner and are sufficiently accurate for practical urposes.

Thus, supposing the same specimen of *Pleurosigma ngulatum* to be measured -

(1) with objective 7 and eyepiece 0,
(2) with objective 4 and eyepiece II.,

nd supposing the length of its image to be sixty-seven nillimeters in the first and twenty-two millimeters in he second case, then, since the actual size of the bject is found by dividing the length of the image, s seen at a distance of ten inches from the eye, by he magnification of the objective and eyepiece com-bined, the length of our specimen of *Pleurosigma ngulatum* is:

(1) $\frac{67}{270}=0.248$ millimeter.
(2) $\frac{22}{90}=0.244$ millimeter.

n all these measurements a tube length of 170 milli-neters must be strictly adhered to.

Pratt's work already referred to[2] would seem to show that there is no known relation between the time required for blood to clot and the number of plates in a given case. Coagulation time must therefore be determined independently of other blood features. The conditions in which blood-clotting is delayed are profound anemia and occasionally the anemia of leukemia, hemophilia, the advanced stage of wasting disease, and profound jaundice, either obstructive or from liver disease.

The two conditions of importance in this list are hemophilia and jaundice because of the danger in operating in these cases. It must, however, be remembered that in jaundice occasionally the test may give *normal coagulation time before operation and fatal hemorrhage occur, nevertheless, after operation.* This is a manifestation of some process of considerable importance but one which is not understood. There may here be some relation to the common post-operative thrombosis in which changes may have taken place in the vessels as well as in the blood.

TABLE VI. TABLE SHOWING THE SOURCE, APPEARANCE, STAINING REACTION, GREEK LETTER EXPRESSING STAIN, AND THE NUMERICAL VALUE OF EVERY CELL FOUND IN THE PERIPHERAL CIRCULATION UNDER NORMAL OR PATHOLOGICAL CIRCUMSTANCES.

	Name according to source.	Name according to appearance.	Name according to stain.	Name according to Greek letter expressing stain.	Numerical value of each cell.
			Protoplasm. Nucleus.		
Non-granular. Erythrocytes.	1.	Red cell.	Oxyphilic	(α)	5,000,000 to cubic millimeter, Found normally in bone marrow only. In peripheral circulation in pernicious and grave secondary anemia.
	2.	Normoblast (Nucleated red cells)	" Basophilic	(α)	
	3.	Gigantoblast or megaloblast (Nucleated red cells)	" "	(α)	
	4.	Plates	Basophilic	(ι)	300,000 to cubic millimeter.
			Granules. Nucleus.		
Granular. Leucocytes.	5. Lymphocyte.	Small monocular.	Neutrophilic..... Basophilic (Sometimes basophilic granules at periphery.)	(ε)	6,000 to 10,000 in c.mm. 20–30 per cent.
	6. "	Large "	Neutrophilic..... "	(ε)	2–3 "
	7. "	Transitional "	" Basophilic "	(ζ)	2–3 "
	8.	Polynuclear	" in leukemia "	(η)	60–70 "
	9.	Coarse granular. (Eosinophile)	Oxyphilic " (Eosinophilic)	(α)	2–3 "
	10. Myelocyte		Neutrophilic	(ε)	Found in bone marrow only. In peripheral circulation in splenomedullary leukemia.
	11. Mastcell		Basophilic " (Requires dahlia to stain.)	(ζ)	½ of 1 per cent. (Virchow). Increased in leukemia.
	12. Eosinophilic myelocyte		Oxyphilic..... "	(α)	Found in bone marrow only. In peripheral circulation in splenomedullary leukemia.

NOTE.—The mast cell of Cornhill was described by him prior to Ehrlich's observations upon the staining peculiarities of these cells, and may have been a myelocyte or a large mononuclear, and had best, therefore, be dismissed from the list of blood cells.

VII. BLOOD-CLOTTING.

The fact that normal blood requires a fixed time or clotting, and that in certain diseases this time varies, makes the phenomenon of blood-clotting of clinical value. However, in the description of apparatus and technique employed in the clinical examination of blood, the discussion of the various causes, etc., producing this phenomenon can have no place. Text-books on physiology and the article on *Coagulation* should be consulted for information on this subject. Therefore, beyond describing the apparatus employed and mentioning the diseases in which variations in the time required for clotting occur, the subject will receive no further consideration.

1. APPARATUS AND TECHNIQUE EMPLOYED IN MEASURING COAGULATION TIME OF BLOOD.—Three methods for determining the rate of coagulation may be employed: (1) The rough test, in which two drops of blood, as nearly equal in size as possible—one from the case under observation and one from a normal individual—are compared as to clotting time. (2) That in which Brodie and Russell's[23] apparatus is employed. (3) That in which Wright's coagulometer tubes are employed.

1. *The Rough Test.*—A drop of blood from the case under observation is received on a glass slide, and simultaneously a drop as nearly as possible of the same size as that from the suspected case is taken from a normal case and placed upon another glass

slide. The time at which the operation is begun is noted. The two slides are placed side by side, and by means of a pin touching the edge of the drop, the stage of the process of clotting is ascertained from time to time. The moment of complete clotting is determined when the pin, being drawn from within outward, no longer leaves a small projection at the periphery of the drop. The time is noted and compared with that of the normal blood. This is a test by comparison. The actual time should not be taken.

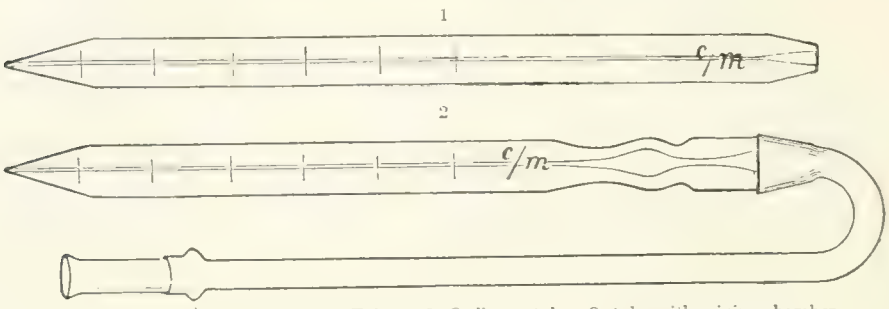


FIG. 804.—Wright's Coagulometer Tubes. 1, Ordinary tube; 2, tube with mixing chamber.

2. *Brodie and Russell's Coagulation Chamber.*—This consists of a truncated glass cone which fits into a chamber. A space exists between the tip of the cone and the bottom of the chamber. Into this space a tube projects connected with a rubber tube. The blood is received upon the tip of the cone so that the tip is entirely covered. The cone is then placed in the chamber and the whole placed under the low power of the microscope or any low power lens.

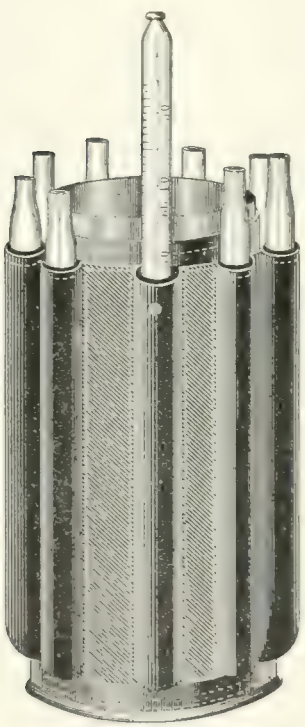


FIG. 805.—Case and Warm Chamber for Wright's Coagulometer Tubes. Chamber for warm water in center surrounded by leather jacket containing tubes and thermometer.

The corpuscles will be seen in slow motion and for the most part separate from each other. The tube is now gently blown through and the corpuscles will be seen to rotate. The time at which this blow is given is noted and thirty seconds later another blow is given. This process is repeated till the blow fails to cause the corpuscles to rotate. The cone is now removed and the blood touched with filter paper. The beginning of clotting is determined by noting when the blood is not taken up by the filter paper and the time measured accordingly. The temperature of the atmosphere and of the instrument will influence the clotting time. With this instrument the time for clotting is found to be from five to eight minutes.

3. *Wright's Coagulometer Tubes.*—In this test, equal quantities of blood are taken by means of accurately graduated tubes. These tubes are blown through, one after another, until that tube is reached which cannot be blown out, and in which, therefore, the contained blood has clotted. The time from the taking of the blood to the moment when the blood has clotted is noted, and this is termed the "coagulation time."

Wright's coagulometer tubes are of two kinds (Fig. 804): 1. Those for testing the coagulation time of the blood. 2. Those for testing the coagulation power of certain substances.

1. *Those for Testing the Coagulation Time of Blood.*—These tubes have a centimeter scale, six centimeters in all, and are shaped as seen in Fig. 804. There are eight such tubes in a set. There is also a round tin receiver, surrounded by a jacket, in which there are nine pockets—eight for the reception of the tubes, the ninth being for the reception of a thermometer (Fig. 805). This part of the apparatus is for the purpose of heating the tubes to blood heat before use by placing heated water in the center tin. This is not essential, as the normal blood is found to be coagulated in the same time without previous heating of the tubes as when such heating is carried out. If heating is resorted to, the thermometer should register 18.5° (half blood heat), or, if clotting is very slow, 37.0° (blood heat).

The test is made as follows: The tubes, as seen in the illustration (Fig. 804), are laid out (if the heating tin is not used) on a sheet of white paper on a table at the bedside. An open watch is also laid upon the table. A fairly large puncture is made in the skin in the usual way. A rubber tube with mouthpiece (similar to that used with the Thoma-Zeiss mixer) is attached to the first tube and blood is drawn up to the fifth division, the time by the watch being noted. Taking the point of the tube away from the blood drop, the column of blood is drawn up to the sixth marking, thus removing the end of the column from the immediate influence of the air. This tube is laid upon the white paper, and the moment at which the observation is begun noted down. In about half a minute the second tube is treated in the same way, in another half minute the third, and so on for the whole set. After the lapse of about one minute the first tube is gently blown through; if the blood is still liquid the second tube is blown through; and so on until a tube is reached from which the blood cannot be blown. The time at which this condition is observed is at once noted and compared with the time, as marked on the paper, at which the observation of the blood in that tube was begun. The difference between the two numbers constitutes the time required for this specimen of blood to clot, and is therefore the "coagulation time." *The time is taken from the moment the blood is drawn into the tube to that at which it cannot be blown from the tube.*

2. In using the instrument to determine the coagulation power of certain substances, the tubes with the mixing space are employed (see illustration, Fig. 804, 2). The substance to be tested is drawn up to one of the divisions on the tube, say the second. Blood is then also drawn up, and the blood and substance to be tested are thoroughly mixed in the mixing space. Unmixed blood is now drawn into another tube, and the different coagulation times for the two tubes are noted. Prof. Wright ex-

hibited at the Paris Congress, August, 1900, an improvement upon this instrument.

Cleansing the Tubes.—This is one of the annoyances of the Wright tubes, for unless cleaned *at once* the tubes become hopelessly clogged. It is well, therefore, to have an attendant draw clear water into each tube the moment the observation has been made upon that tube. It is evident that as the observer is occupied with his observations, those tubes already tested, and containing traces of blood, will become dried out and clogged. A wire should be passed down the tubes to break up the clotted blood.

When *all trace* of blood has been removed, and *not till then*, ninety-five per cent. alcohol should first be drawn through the tubes, and afterward ether. The tubes will then be ready for use again. The importance of prompt action in the matter of cleaning the tubes cannot be too emphatically stated; disregard of this promptness will render the tubes useless.*

2. Clinical Value of Observing Coagulation Time of Blood.—The normal coagulation time is from two to eight minutes. The following table shows the differences in coagulation time in various diseases.

Coagulation Rapid.	Coagulation Delayed.
Malignant disease: inflammation or sloughing in progress.	Malignant disease: uncomplicated.
Pneumonia.	Jaundice (important in operation for gallstones, as one of the most common complications causing fatal results is postoperative hemorrhage due to reduced coagulability of the blood.
Hemoglobinemia: in severe grade of malaria; in severe grade of septicemia; in yellow fever; in typhus fever; in burns.	Obscure conditions associated with frequent attacks of epistaxis: hemophilia; scurvy; erythema multiforme; pernicious anemia; anemia delayed in accordance with severity; purpura hæmorrhagica.
Poisons: snake poisoning; chlorate of potassium; antipyrine and acetanilide; hydrocyanic acid; phenacetin; phosphorus; carbonic acid; illuminating gas.	

The coagulation time may be increased by:

1. Inhalation of carbonic acid gas.
2. Ingestion of calcium chloride.
3. The gelatin treatment for aneurysm. (*a*) Lancereaux's method: four to five grams white gelatin dissolved in 200 c.c. of 0.7 per cent. sodium chloride solution and sterilized at 120° C. (*b*) Futcher's [24] method: 250 c.c. of one-per-cent. gelatin solution in normal salt solution.

3. Detection of Blood when in Small Quantities.—For full information upon the more complicated apparatus and technique (spectroscopic and chemical) employed in the detection of blood for medicolegal purposes, the reader is referred to the article on *Blood Stains*.

A simple clinical test is the following: Allow a few drops of the fluid supposed to contain blood (urine, gastric contents, etc.) to dry upon a glass slide. Add to the margin of the dried fluid a few grains of common salt. Now from a pipette allow a drop or two of glacial acetic acid to attack the salt and dried fluid. Gently heat the slide until the acid has dried entirely; examine with low power. If blood is present crystals of hemin will have formed. Hemin is a derivative of hematin (or hydrochlorate of hematin) which is thus produced. If no blood be present no crystals will be formed.

* The Wright apparatus may be had of Alfred E. Dean, 73 Hatton Garden, London, E. C., for £2 5*s*; the improved instrument of T. Hawksley, 357 Oxford Street, London, for £1 15*s*.

VIII. Viscosity of the Blood.

The viscosity of the blood may be determined by the Hess viscometer. This consists of two graduated glass tubes fastened upon a bit of opaque glass. These two tubes of capillary bore are connected at their lower end by a third tube which connects with a rubber bulb. Distilled water is placed in one tube which, by means of a stopcock can be shut off from the other tube. Into a detachable portion of the tube is placed the blood which is drawn in by capillary action. The cock shutting the tubes in now opened and by suction with the rubber bulb the water and blood flow through the graduated tubes till the blood reaches the mark 1 on the scale when suction is discontinued. The reading is taken by observing the height of the water which indicates the viscosity of the blood under observation compared with that of distilled water. The instrument is cleaned by forcing the contents out by pressure on the bulb and washing through with ammonia. Viscosity in men is about 4.55, women, 4.51, depending upon "the number of red cells, hemoglobin contents, the gaseous richness and on protein, fat, and salt in the blood."

The diseases in which variations from normal are found are the anemias (blood and plasma), leukemia, hypoviscosity of blood and hyperviscosity of plasma. Polycythemia, hyperviscosity (blood and plasma). In nephritis, hypoviscosity of blood and hyperviscosity of plasma "the former due to anemia, the latter to retained products of metabolism." For further discussion see an article by Austriau[25] in the Johns Hopkins Hospital Bulletin for January, 1911.

IX. Cryoscopy, the Freezing-point of Blood.

As yet this observation has yielded little to aid in diagnosis. The underlying principle of this observation is that the freezing-point of any liquid in which is dissolved a substance is lowered to a degree proportional to the concentration of the solution. On this basis it was hoped that products of catabolism in the blood would manifest themselves through variations in the freezing-point. Unfortunately, however, the freezing-point is readily influenced by many factors difficult to control and determine. Thus cyanosis from any cause produces great variations in the freezing-point. The blood (and urine) moreover contain bodies in solution varying greatly in proportions and varying in associations, factors which will greatly influence the freezing-point. The only promise of assistance in diagnosis from this method is in nephritis. The reader is referred to the article on *Cryoscopy* for further information as to its value and the technique of the test.

X. Alkalinity of the Blood.

Engel's[26] (*Berliner klin. Woch.*, 1897) modification of the Löwy-Zuntz method for estimating the degree of alkalinity of the blood places the apparatus among those applicable for this purpose in bedside examinations. It consists of the following (Fig. 806):

1. A capillary pipette similar in construction to that used in the Thoma-Zeiss corpuscle-counting apparatus, but of somewhat larger size. The capillary portion is marked off into ten equal divisions. The fifth mark indicates 0.025 c.c. and the tenth indicates 0.05 c.c. Above the bulb portion is a mark that indicates 5 c.c.
2. A receiver and a stirrer made of glass.
3. A burette measuring 5 c.c., and marked 1, 2, 3, 4, 5 in equal divisions.
4. Litmus paper.

To Make the Test.—Blood from the ear (taken in the usual way) is drawn up to the 0.05 mark and distilled water to the 5.0 mark. These are mixed by carefully shaking the pipette, and then the mixer is blown out into the glass receiver. In the burette is placed a $\frac{1}{5}$ normal tartaric acid solution.

As stated elsewhere in this article, a normal solution in chemistry is the sum of the atomic weights of the chemical employed (in grams) in 1,000 c.c. of distilled water. The formula for tartaric acid is $C_4H_6O_6$, and the sum of its atomic weights would be $\frac{C_4H_6O_6}{2} = \frac{48+6+96}{2} = 75$. Therefore 75 grams of tartaric acid in 1,000 c.c. of water would represent a normal tartaric acid solution. A $\frac{1}{75}$ normal solution, however, is all that is required, which would be one gram tartaric acid to one liter of distilled water.

This solution is then allowed to drop from the burette into the receiver containing the diluted blood, which is stirred from time to time with the glass stirrer. Blue litmus is immersed from time to time, and directly this turns red, showing an acid reaction, the titration is at an end, and the amount of acid solution required to accomplish this acid reaction (that is, the amount required to overcome the alkalies

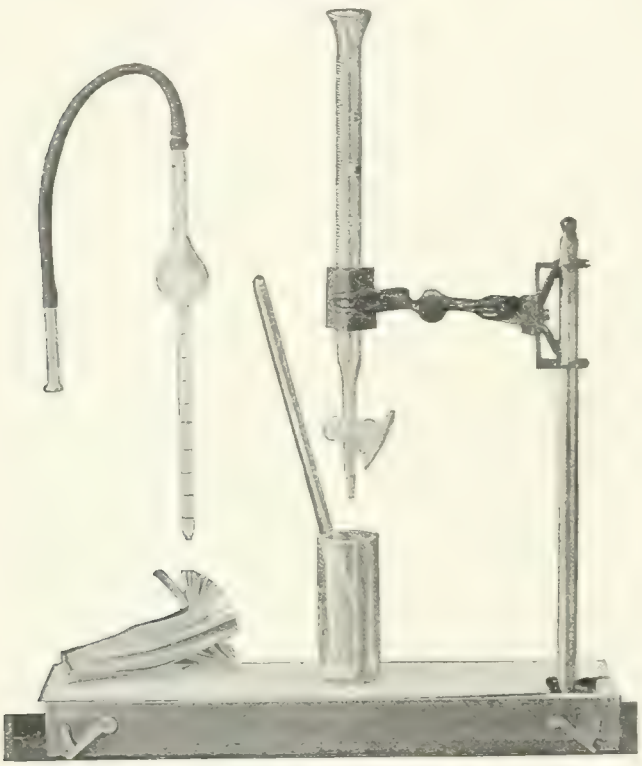


Fig. 805.—Engel's Apparatus for Determining at the Bedside the Degree of Alkalinity of the Blood. 1, Capillary pipette for taking and mixing definite quantities of blood; 2, burette for acid solution; 3, litmus paper; 4, receiver and stirrer for diluted blood while titrating.

of the blood) is ascertained by noting the level at which the liquid stands in the burette.

There is no one alkali in the blood which we can hold responsible for its alkaline reaction. It is therefore necessary to measure this alkalinity by taking a known alkali, say NaHO, as the unit. By ascertaining the amount of a $\frac{1}{75}$ normal tartaric acid solution required to neutralize a known quantity of blood, and then ascertaining the amount of sodium hydrate neutralized by this amount of a $\frac{1}{75}$ tartaric acid solution, we learn in terms of NaHO the amount of tartaric acid required to neutralize a known quantity of blood. Things which are equal to the same are equal to one another.

Thus by experiment we find that 0.5 c.c. of $\frac{1}{75}$ normal tartaric acid solution neutralizes 0.05 c.c. of blood; then 1,000 c.c. of $\frac{1}{75}$ normal tartaric acid solution neutralizes 100 c.c. of blood.

Again, by experiment, we find that 75 grams of tartaric acid neutralize 40 grams NaHO ($23+1+16=40$). 1 gram of tartaric acid neutralizes ($\frac{1}{75}$ of 40) .533 milligrams of NaHO.

Since 1,000 c.c. of $\frac{1}{75}$ tartaric acid solution neutralizes 100 c.c. of blood, 100 c.c. of blood has an alkalinity of 533 milligrams of NaHO.

0.5 c.c. of $\frac{1}{75}$ normal tartaric acid solution neutralizes 0.05 c.c. of blood. 1,000 c.c. of $\frac{1}{75}$ normal tartaric acid solution neutralizes 100 c.c. of blood. 75 grams of tartaric acid solution neutralizes 40 grams of NaHO.

$C_4H_6O_6 = \frac{48+6+96}{2} = 75$ neutralizes NaHO $= 23+1+16=40$. Then 1 gram of tartaric acid solution neutralizes ($\frac{1}{75}$ of 40) 0.533 NaHO.

This is the quantity of tartaric acid in the $\frac{1}{75}$ normal solution (1 gram in 1,000 c.c. of water). This, therefore, is the value in alkalinity—so to speak, in terms of NaHO—of the tartaric acid solution employed.

Now on titration it is found that from 9 to 10 drops of such a solution are required to neutralize 0.05 c.c. of blood. 10 drops equal 0.5 c.c which equals 0.5 gram. 0.5 gram equals 0.266 NaHO. Therefore 10 drops equal an alkalinity of 0.266 NaHO. 1 drop = 0.0266 NaHO.

It is perhaps better to bear in mind that 9 or 10 drops represent the normal, and to report examinations accordingly. For example, "6 drops required to neutralize," "12 drops required to neutralize," etc. It would also simplify the proceeding to use a solution of litmus in the blood solution instead of the papers.

XII. Blood Parasites.

The parasites observable in blood are the malarial parasite, the filaria, and the trypanosome. All of these are observable by the methods already described; for morphological, biological, and clinical information regarding each of these the reader is referred to the appropriate article under each head. By special method the trichinæ can be seen in the blood. This method is described by Herrick and Janeway.[27]

XIII. Bacteriology of the Blood.

1. Technique in Obtaining Blood for Bacteriological Examination.—While one familiar with bacteriology should be appealed to to determine the character of the growth resulting from culture there is no reason to-day why any practitioner should not be competent to procure a blood specimen for cultural purposes. The description here deals only with the technique of taking the specimen.

The skin over a prominent vein at the inner bend of the elbow should be scrubbed with brush and soap and rubbed with alcohol-ether. The veins may be made to stand out by having the patient close his fist and flex and extend the elbow or by bandaging the arm above the elbow. It is rarely necessary to incise the skin but it must be remembered that no amount of disinfecting without incising will rid the deeper layers of the skin of the staphylococcus albus a few colonies of which will in most instances contaminate the growth.

After cleansing the skin it is well to leave for about twenty-four hours a compress soaked in 1–1000 bichloride on the area.

The glass syringe with asbestos packing is that

	Red blood cells	Hemoglobin	Color index	White blood cells	Proportion of red to white blood cells	Poikilocytes	Microcytes and macrocytes	Degeneration areas and polychromatophilia	Normoblasts and granuloblasts	Small mononuclear lymphocytes	Large and transitional lymphocytes	Polynuclear leucocytes	Eosinophilic leucocytes	Myelocytes	Mastcells	Platelets	Fibrin	Coagulation time	Blood dust
1. Normal blood	5,000,000 to c mm.	90 to 100%	1	6,000 to 10,000 to c mm	700 to 1	Absent	Absent	Absent	Absent	20 to 30 in every 100 leucocytes; 20 to 30%	6 to 8 in every 100 leucocytes; 6 to 8%	60 to 75 in every 100 leucocytes; 60 to 75%	2 to 3 in every 100 leucocytes; 2 to 3%	Absent	1 in every 400 leucocytes; $\frac{1}{4}$ of 1%	300,000 to c mm	Absent	2 to 3 minutes	Present
2. Primary anemias																			
A, Chlorosis	4,000,000 to c mm normal	Below 80% reduced	Low	Normal	Normal	Present	Present	Present	Absent	Normal	Normal	Normal	Normal	Absent	Normal	Normal	Absent	Normal	?
B, Pernicious	1,000,000 to 3,000,000 to c.mm.; markedly reduced	Reduced, but above the reduction in red cells	High	Normal	Altered from normal 300 to 1	Present	Present	Present	Present	Increased 30 to 40%	Normal	Decreased 50 to 60%	Normal	Absent	Normal	?	?	?	?
3. Secondary anemia (Note 1)	2,000,000 to 4,000,000 to c.mm.; reduced	Reduced in proportion to decrease in number of red cells	Fairly high	12,000 to 15,000 to c mm; moderate increase	Altered from normal 400 to 1	Present	Present	Present	Absent	Normal or decreased in proportion to polynuclear increase	Normal	Increased 75 to 80%	Normal	Absent	Normal	?	?	?	?
4. Addison's disease and 5. Hemochromatosis	Normal, may be slight anemia	Normal	According to grade of anemia	Normal	Normal	Absent	Absent	Absent	Absent	Normal	Normal	Normal	Normal	Absent	Normal	Normal	Absent	Normal	Present
6. Anemia, pseudoleukemia infantum (Note 2)	Reduced	Reduced	do.	Greatly increased 100,000 to c mm.	Altered, 18 to 1	Present	Present	Present	Present	Increased	Normal	Decreased	Normal	Present	Normal	?	?	?	?
7. Leucocytosis																			
A, Leukemia																			
(1) Lymphatic	Normal or slightly decreased	Normal or slightly diminished	do	Marked increase, 70,000 to c mm	Altered, 30 to 1	May be present	May be present	May be present	Not present unless anemia exists	Increased 70 to 80%	Normal or slightly increased	Decreased	Normal	Absent	Normal	?	?	?	?
(2) Splenomedullary or lienomyelogenous myelocytic	Normal or slightly decreased	Normal or slightly decreased	do	Very greatly increased 150,000 to c mm.	May be as low as 1 to 1	May be present	May be present	May be present	Not present unless anemia exists	Decreased	Normal	Decreased	Normal	Present	Increased	?	?	?	?
B, Inflammatory Polynuclear	Normal	Normal	do	Increased 12,000 to 40,000 to c mm.	Slightly altered	Absent	Absent	Absent	Absent	Decreased	Normal	Increased 75 to 80%	Normal	Absent	Normal	?	?	?	?
C, Trichinotic, etc Eosinophilic	Normal	Normal	do	Increased	Normal	Absent	Absent	Absent	Absent	Normal	Normal	Decreased	Increased as high as 80%	Absent	Normal	?	?	Normal	?
8. Hodgkin's disease	Normal May be reduced	Normal May be reduced	do	Normal	Normal	Absent May be present	Absent May be present	Absent May be present	Absent	Normal	Normal	Normal	Normal	Absent	Normal	?	?	?	?
9. Splenomyelia Polycythemia... Note 3)	6,000,000 to 13,000,000	120% to 150	1	4,000 to 20,000	1,200 to 1	May be present	Absent	May be present	Not rare	Decreased	Decreased	Increased	Absolute increase	Rare	?	?	?	?	?

Note 1. The anemias due to certain intestinal parasites (*Ankylostoma duodenale*, *Bothriocephalus latus*) are, except for especial features, indistinguishable from primary pernicious anemia. The finding of the parasites settles the diagnosis. For features of chloroma and other leukemias see description under the appropriate headings in this Handbook.

Note 2. Some doubt exists as to whether this is not one of the recognized anemias presenting peculiar features because occurring in a child. It must be remembered that blood of infants and young children presents very varied features.

Note 3. Other names given to this disease are Vaquez's or Osler's Disease—Myelopathic Polycythemia, Cryptogenetic Polycythemia.

Note 4. The blood parasites may be included in this table. 1. Malaria, 2. Filaria, 3. Spirochete, 4. Trypanosome, 5. Trichina (by special method).[27]

most employed for sterilizing. Dry heat is preferable and should be employed at 150° C. for an hour. This is superior to the use of *any* chemicals or to boiling in water. A bit of gauze sterilized at the same time can be wrapped about the syringe for transportation or the syringe with the needle can be carried in a large test-tube with cotton at the bottom and plugged with cotton. It is important that the needle be very sharp and protected from any dulling influences. Many failures to get into the vein are due to a slight blunting of the point causing the needle to slip about the vein. Five or six tubes plugged with sterile cotton and containing melted agar at 45° C. should be at hand. The needle is now plunged through the skin, then through the vein in the direction of the blood stream. When in the vein the blood will at once flow into the lower portion of the syringe and gentle traction of the piston will fill the tube—5 to 20 c.c. of blood are required. It is well to ascertain from the bacteriologist how much he will wish introduced into each tube, for the quantity required differs according to the organism suspected. The blood after being promptly mixed is poured into sterile Petri dishes and transferred to the incubator. These steps should all be carried out with the least possible delay. The chief sources of contamination in growths are: 1. Imperfect disinfection of the skin; 2. lack of thorough asepsis of the apparatus; 3. delay in transferring specimen from syringe to medium; 4. delay in transferring preparation to incubator; 5. exposure to air; 6. variations in temperature.

2. The more important Blood Organisms detectable by Blood Culture are: 1. Streptococcus—several varieties; 2. staphylococcus—several varieties; 3. pneumococcus—possibly several varieties; 4. gonococcus; 5. typhoid bacillus—several varieties; 6. *Bacillus aerogenes capsulatus*.

XV. Classification of the Leukemias.

The following classification of the leukemias accords with the clinical and laboratory manifestations of the disease. Some features of this classification are open to discussion, but it is the most satisfactory so far offered.

Classification of the Leukemias.

I. Lymphatic.	Always chronic.		
II. Myelogenic ...	*a.* Acute lymphoid *b.* Acute myelocytic *c.* Chronic myelogenous *d.* Chloroma *e.* Myeloblastomata with Bence Jones albumin		Myeloblastomata.

Note.—The lymphoid marrow cell is the megaloblast of Naegeli.

XVI. Chart Arranged for Clinical Report on the Blood.

Name Record No.

Address

Red Blood Corpuscles:

Size	Normally 1 [illegible] of an inch, 7 μ.	
	Microcytes, [illegible]	
	Macrocytes, 8–10 μ.	
Shape	Normally, biconcave discs.	
	Poikilocytes, irregular outline.	
	Crenated, spiculated.	
Color.	Normally, pale yellow.	
	Colorless, shadow corpuscles.	
	Vacuolated, degeneration areas—deficiency in hemoglobin.	
Number per cubic millimeter.	Normal, 5,000,000.	
	State instrument used.	
Nucleated red cells.	Normally, not present.	
	Normoblasts.	
	Megaloblasts or gigantoblasts.	
Staining	Normally uniform.	
	Polychromatophilia = different intensity of stain in cells	

Other staining features.....
State stain used.....

Malarial parasite.	Hyaline.	Ameboid.....	
		Non-ameboid.....	
		Pigmented.....	
	Pigmented.	Intracellular	One-fourth grown.
			One-half grown....
			Full grown.....
			Pigment motile....
		Extracellular.	Non-flagellating...
			Vacuolated
			Flagellating.....
			Non-vacuolated
			Pigment [illegible]
	Segmenting		
	Crescents.....	Pigment motile...	
		Flagellating	
	Round bodies..	Pigment motile...	
		Flagellating	
	Stained specimen.....		
	Mention characteristics.....		
	Conclusion.		
	Type of infection		
	Single, double, multiple, or mixed infection?....		
	Age of parasites.....		
	Sex of parasites		
Other blood parasites.	.....		

Hemoglobin:
Normal, 85 to 95 per cent.....
State instrument used.....
Color index.....
Volume index.....

White Blood Corpuscles:

Number per cubic millimeter.	Normal 6,000 to 10,000.	
	State instrument used ...	
		Normal.
Number per each 100 leucocytes.	Small mononuclear lymphocytes	20–30 %
	Large mononuclear lymphocytes.....	3
	Transitional lymphocytes.....	3
	Polynuclear leucocytes	60–70
	Eosinophiles	2 4
	Mast cells.....	0.25
	Myelocytes	not present
	Eosinophilic myelitis.....	not present.
Plates.	Present (normal, 250,000 per cubic millimeter)....	
	Absent	
Phagocytes	Present	
	Absent	
Fibrin.....	Present.....	
	Absent	
Coagulation.	State instrument used....	
Additional features and tests.....		

C. N. B. Camac.

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Blood-letting.—This title includes all methods of abstracting blood for therapeutic purposes, whether they are for a general or for a local effect. The terms *venesection* and *phlebotomy* are restricted to bleeding from the larger veins, for the purpose of influencing the system generally; while *leeching*, *wet-cupping*, and *scarification* are means of abstracting blood from the capillaries, the effect of which is almost entirely local. *Arteriotomy*, the abstraction of blood directly from an artery, usually the temporal, has been resorted to, but is now abandoned as a therapeutic measure.

Venesection is of very ancient origin. References to it have been found in history prior to the time of Hippocrates, and in the writings of this early authority it occupies an acknowledged position as a valuable therapeutic agent. During the many years that it has been employed it has been viewed with a varying degree of favor, and at various periods its advocates have employed it in all forms of disease and in a most extravagant manner. The seventeenth century and the early part of the last century mark the periods of its greatest use, during which excessive and repeated bleedings were constantly employed. It was not only in the acute inflammations and sthenic fevers that it was resorted to, but was used in every form of illness and in many debilitated and weakened conditions which we now know must have been most injurious. The strong and healthy also applied for it to relieve the effects of overindulgence with much the same freedom and confidence that they now resort to a dose of epsom salts. In the fourth decade of the last century there arose a world-wide reaction against this excessive use, the practice fell into disrepute, and within a few years it had returned within more rational limits. With the advance of our knowledge of physiology and more careful clinical observation, its employment became based on a scientific foundation. It was used with a definite purpose in view and restricted to certain well-recognized conditions. As a therapeutic agent, it has never been abandoned. The older members of the profession, who are familiar with its use, find many occasions in which it proves of service, and recent investigations and more frequent references in medical literature indicate a revival in its favor.

Venesection exercises what may be termed a mechanical effect upon the circulation, as well as a general effect upon the system. When a certain proportion of the blood is removed the tension of the blood-vessels is at once lessened, the degree depending upon the amount withdrawn. This effect is but temporary, as that which is lost is rapidly renewed; but, if any disturbance of the circulation exists, it is sufficient to allow the equilibrium to be regained, the heart beating more easily and the blood flowing more freely through the vessels.

The general effect upon the system is of the utmost importance. Accompanying the lowering of blood pressure and loss of blood cells, there is a diminished activity of the various functions. The heart's action is quieter, respiration goes on more slowly, tissue changes are less active, and there is a lowering of body heat. This depression is but temporary. In a few hours there begins a renewal of the blood, tissue changes are accelerated, the nervous system is improved by a stimulation of the nerve centers, and general bodily improvement is the result. At the International Medical Congress of 1900, in the discussion upon this subject, M. A. Robin stated, as the result of many years' observation, he was satisfied that after moderate bleeding of 150 to 250 grams, polyuria is regularly observed, and the excretion of solids is increased. A greater amount of air is taken into the lungs, as much as sixty-one per cent., and the proportion of oxygen consumed by the tissues is correspondingly increased. When the bleedings are renewed this reaction is slower, and when they are frequently repeated, a state of anemia ensues, with a tendency to degenerative changes. Since that date our knowledge of the effect of blood-letting has made rapid strides. During the first few years of this century Roux demonstrated that the abstraction of blood from animals produced a rapid formation and increase in antitoxins and where a condition existed that caused a decline of these bodies, bleeding at once checked such fall and there followed a reformation. A few years later, Schroeder of Copenhagen published observations on typhoid and allied fevers in man, showing that bleeding up to twenty ounces, also here increased the specific agglutinating properties of serum, and, as in animals, under certain conditions where the agglutinating properties had begun to decline, blood-letting checked such decline and produced a marked increase in this power. These observations have been of some practical value in the production of antitoxins, but so far have not been taken advantage of to increase our therapeutic knowledge.

Indications.—The indications for bleeding may be summed up under three heads: (*a*) when there is excessive vascular tension; (*b*) when it is desired to obtain the benefit of its physiological action upon the various tissues and organs; (*c*) when it is believed that good may result from removing a definite amount of blood, and with it a certain proportion of toxic material, from the system.

There is no difference of opinion as to the value of venesection in all conditions in which there is venous engorgement. It may be desirable to try the nitrites and allied drugs for the purpose of "bleeding into the arteries," or to employ hydragogue cathartics or diuretics to unload the congested vessels; but where these measures fail, bleeding is always indicated. The cause of the obstructed circulation may lie in the heart or in the pulmonary tissue. The effect of either of these causes is an overfilled and possibly a dilated right heart, distended veins, and more or less congestion of the various organs. In this condition the removal of blood from the venous system affords prompt relief. The laboring heart beats more freely, the arteries become filled, and the congested veins and organs return to the normal. The dyspnea disappears, the dusky hue of the skin fades, and the general condition of the patient is at once improved. Mitral disease, when compensation is failing, and a feeble heart that is suddenly overtaxed, are the two conditions that most frequently give rise to these distressing symptoms. In such cases, when the dilatation is extreme and the force of the heart very low, venesection must be prompt to be of service. Of the pulmonary causes of venous congestion, emphysema is the most common, and in this condition marked benefit will follow the withdrawal of blood. Where there is a tendency to pulmonary edema it affords favorable conditions for this treatment.

Venesection is also of service when the arteries

show a condition of increased tension, when the pulse is full and bounding, and when a condition of general plethora prevails. In these cases the relief afforded by the withdrawal of blood is very marked, the reduced blood pressure relieving the congested organs and often preventing cerebral hemorrhage. When hemorrhage has taken place, it is always indicated, as the more rapidly the blood pressure is lowered, the more favorable is the condition of the patient. If there is a suspicion of a thrombosis more caution must be observed as too great lowering of blood pressure will favor an increase of this trouble. In the convulsions of uremia, and especially in puerperal eclampsia, when there is high arterial tension, the value of venesection is unquestionable. The relief is immediate, and the severity of subsequent attacks is likely to be lessened. In puerperal states there should be no hesitation in resorting to it, if the arterial tension is abnormally high; and the fact that a free loss of blood has occurred during labor does not warrant the belief that venesection will be any less effective in relieving the tension. In these cases much of the benefit is due to the reduction of blood pressure, and much also may be explained by the favorable influence exerted on the tissue changes and by the increased oxidization.

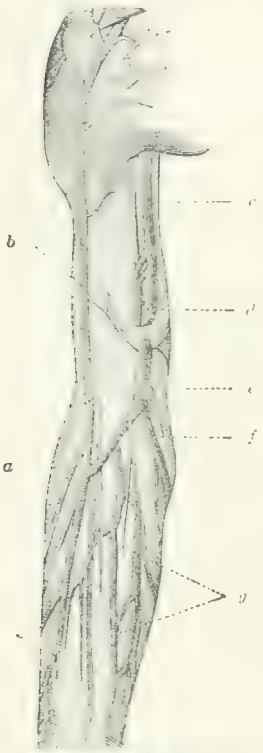

FIG. 807.—The Superficial Veins of the Forearm; Skin Removed. *a*, Median cephalic; *b*, cephalic; *c*, brachial; *f*, median basilic; *g*, anterior ulnar; *d*, median nerve.

It is difficult to determine to what extent the benefit should be ascribed to the actual removal of toxic material from the body (with the blood that is drawn off), yet we find that there are many eminent authorities who lay great stress upon this explanation. To increase the usefulness of the procedure in these toxic cases, it is recommended that the bleedings should be very free and that the blood lost should be replaced by normal saline solution, either administered subcutaneously or injected directly into the veins.

The effect of venesection in lowering temperature and allaying the symptoms of inflammation, together with the more recent knowledge of the increased antitoxic properties of serum after the withdrawal of blood, would suggest the wisdom of employing it in the treatment of fevers and inflammatory diseases—a practice which was so much in vogue at the time when venesection was used empirically. This proposition, however, does not meet with favor. It is maintained that the relief afforded is but temporary, and that the tendency to fatty changes, present in pyrexia, is heightened by the repeated withdrawals of blood. The symptoms undoubtedly show marked improvement immediately after the operation, but the greater debility which results and the prolonged convalescence prevent its general acceptance. The only acute disease in which venesection receives much attention is pneumonia. In addition to the benefits derived from the lessening of the plethora and the easing of the overworked heart, the lessening of the inflammatory process and the probable limiting of the extent of the consolidation must also be considered as results of some value. Numerous cases have been reported in which venesection has proved serviceable. When it is resorted to at the outset, in a plethoric patient with sthenic symptoms, a full pulse, difficult respiration, pain, and fever, it acts most favorably, and there is every reason to believe that it renders the attack less severe. Frequently recourse is had to venesection too late in the disease, as a last resort, and although the distressing symptoms may be allayed for the moment, the ultimate result is rarely favorable.

FIG. 808.—Forearm with Ligature Applied. Finger at junction of median basilic and median cephalic veins.

Method of Procedure.—Formerly, blood was withdrawn from the veins of the arm, the external jugular, the veins beneath the tongue, the scrotal veins, and the veins of the leg; but at the present time a vein on the anterior surface of the forearm is the one chosen, unless some particular reason exists why another should be selected. The veins in this region that become most prominent, when the circulation in them is arrested, are the median cephalic and the median basilic. The former is the proper one to select, as the median basilic is in close relation to the artery. The median cephalic is external to the tendon of the biceps and away from any region of danger. It will be found, however, that the size and prominence of the veins in front of the elbow vary greatly, and generally the most marked one is selected regardless of its name or position.

FIG. 809.—Glass Leech Tube.

In performing the operation strict antiseptic precautions should be observed in the preparation of the site and in the selection of the knife and dressings. The arm is allowed to hang suspended and a firm bandage is applied above the elbow, sufficient force being employed to compress the superficial veins, and yet not enough to intercept the arterial flow. The vein is opened either longitudinally or in a direction slightly oblique to the axis of the vessel, the point of the blade being inserted directly into the vessel and withdrawn with a downward cutting motion. Before one makes the incision he should place the thumb of the left hand below the point of opening, in order to secure the vessel firmly. Care must also be observed that the skin is tense and in its proper relation to the vessel, otherwise the incision through the skin may not coincide with the opening into the vein, and instead of a free flow of blood there will be only an exudation of blood into the cellular tissue. As soon as the blood flows freely, the pulse of the other arm and the patient's face should be kept under observation to determine the effect on the circulation and to detect any symptoms of syncope. Ten to thirty, or even forty ounces should be removed, according to the

condition and temperament of the patient. The quantity taken should always be sufficient to make a decided impression upon the circulation. Frequently the amount withdrawn does not exceed a few ounces. This is too small a quantity to afford any benefit to the patient, and as a further result venesection is discredited. When sufficient blood has been removed the flow is readily checked by applying a compress over the incision, removing the constricting band, and bandaging the arm, which bandage may be removed in twenty-four hours.

It is often desirable to abstract blood from some prominent part for the purpose of relieving a local hyperemia or congestion, as in many bruises and ecchymoses, in disease about the eye, nose, ear, gums, etc., and in some forms of cellulitis. Such local blood-letting is occasionally employed to lessen the congestion and pain of deep parts by withdrawing blood from the surface of the body near to the affected area, as in pleurisy, pneumonia, sciatica, etc. In all cases the blood flows from the capillaries or superficial vessels, and the quantity is very slight in comparison with that which is abstracted in general blood-letting. To accomplish this end, leeches, scarification, and wet-cupping are the means employed.

Leeching.—This means of locally abstracting blood is still frequently employed, but not to such an extent as formerly. When any large anount of blood is required, a number of leeches must be used. A single leech will absorb from two to three drams of blood, and this may be increased as much more by warm fomentations applied after the leech has dropped off. The leeches may be placed in a wine glass which should then be inverted over the desired spot. If the area is very limited, or if the blood is to be withdrawn from the nasal cavity, gums, or any cavity, a leech glass should always be utilized. The leech will bite more freely if removed from the water an hour or more before needed, and for the same reason the part should be thoroughly cleansed. When a leech shows no inclination to bite, rubbing the skin with sweetened water will sometimes induce it to fasten upon the spot. The peculiar bite of the leech always leaves a permanent scar, and care must be observed in selecting a site which is not conspicuous.

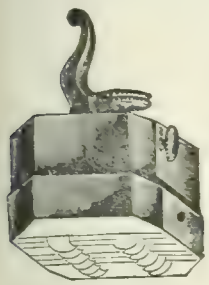

Fig. 810.—The Scarificator.

Scarification and Wet Cupping.—By these means blood is abstracted through small superficial incisions into the skin, the flow being augmented by the cupping glass when that instrument is employed. The incisions may be made with an ordinary knife or lancet, or by means of a scarificator. In the latter instrument the blades may be adjusted to any desired length so that the cutis vera of the part may be incised without penetrating to the deeper tissues. The cupping glass may be one of those specially constructed for this purpose, or an ordinary wine glass may be made to serve the same end. The cavity of the glass is heated over a spirit lamp, or by burning a small quantity of spirit in it, and then the glass is quickly inverted over the desired part and placed in such a way that the air will not enter. As the heated air cools its density is increased and suction force is exercised upon the incised surface. The glass should be removed as soon as it ceases to act and a fresh one applied. A cupping glass with a rubber bulb attached, on the principle of the ordinary breast pump, is also utilized. (See *Cupping.*)

Beaumont Small.

Blood Pressure.—The observation of blood pressure represents one of the most striking advances of modern clinical medicine, and one does not go far into the study of circulatory disease without discovering that alteration of pressure in the blood-vessels constitutes one of the most conspicuous facts in cardiovascular disease. The chief function of the elaborate circulatory mechanism is to maintain high pressure or bring about low pressure in one part or another of the blood supply of the body.

The maintenance of the circulation is not a question of the degree of tension in any part of the circulatory system, but of a proper relation in tension between pressure in the arteries, where the blood is stored, and the points at which it is needed. It is usual, however, to study the question from the standpoint of the arteries. In most cases it is only late in circulatory disease that venous pressure becomes of importance. The freedom of passage between the arteries and veins through the arterioles and capillaries is of extreme importance.

The effect of muscular exercise on blood pressure is at first to raise arterial pressure, but finally, after the exercise has been continued for some time, the pressure falls again to normal. The same is true in regard to the effect of mental effort. During the existence of this increase of arterial pressure due to exercise, there is a large amount of blood in the arteries. This is obtained from the large veins in the abdomen, which act as a reservoir from which, in health, blood can be drawn to flush any part of the arterial system. This tide of blood between the digestive organs and the systemic area is illustrated in many ways. Thus, the coldness after eating indicates that the tide has set toward the digestive organs. The indigestion following exercise after eating, and even more markedly the indigestion following strong emotion after a meal, shows that the tide has set the other way. The lethargy and mental inactivity of those who habitually overeat, and the tendency to indigestion of mental workers, indicate the same thing. The relation between the circulation in the abdomen and the circulation in the brain is an intimate one. The proverbially good mental condition in patients suffering from acute peritonitis may very well be due to the spasm of all the abdominal muscles that prevents the accumulation of large quantities of blood in this part of the body.

The impression of the circulation obtained by one's early study of physiology is erroneous. It resembles too closely the idea of a series of closed pipes, as in the plumbing of a house, the water entering at a large pipe, going through a system of smaller pipes, and, after having been used in certain fairly definite receptacles, being collected by a similar set of pipes which convey it to a common outlet. The facts, however, are very different in the human body. The arterial system is really a reservoir of blood in which the area of a cross-section of the combined vessels very rapidly increases from the heart outward. In this series of passages the blood is contained and held under pressure by a muscular envelope. From this reservoir the blood escapes for use, through the arterioles and capillaries, and the office of the heart is to pump into this reservoir sufficient blood to maintain the pressure depleted by the blood used by the capillaries. This naturally creates a flow of blood from the heart toward the periphery, but the immediate use of the heart is to maintain this arterial pressure. This is well shown by the fact that the actual amount of blood propelled by the heart varies greatly, according to the demand for fresh blood on the part of the body. During exercise, when the peripheral vessels are open, and there is a drain on the arterial system, the heart works harder to supply the deficiency. Thus the arrangement and movement

of blood in the body are seen to be more like a system of irrigation than one of circulation, there being a reservoir with numerous branches from which the irrigating fluid is distributed and a system of conduits by which it is collected, to be again transferred to the storage place.

The idea of the office of the veins as a storehouse of blood is a very old one, and one which has had much influence upon therapeutics. The consideration of the arterial system as a similar reservoir in which suitable pressure is maintained by the muscular elements which go to make it up, seems to have been overlooked. The truth of the statement that the arteries form a reservoir rather than mere conduits is shown by the fact that arterial pressure is practically uniform throughout the arterial system. This means that the blood moves with the utmost freedom throughout the arteries, and that its movement is controlled, not by pressure from behind, but by the escape from in front.

The arterial system is thus like a reservoir analogous to the tubular boiler of some types of engines. It is a hollow ramifying organ containing a vital fluid, the capillaries being the ducts. Whenever there is a demand for this vital fluid in any part of the system, the muscular covering of the organ contracts, the arterioles which lead to the proper capillaries dilate, and the demand is supplied. The demand upon this organ for the vital fluid is so great that a special mechanism, represented by the heart, conducts the vital fluid from the places where it is manufactured, and the lungs where it is purified, to the high-pressure receptacle from which it is used. This conception of the arterial system as a high-pressure receptacle for the blood is well borne out by a study of the evolution of the circulation in the lower forms of life, where there are first found small interstices in the tissues through which the blood ebbs and flows in an irregular manner. As we ascend the scale the blood is found in more definite receptacles, until finally we reach the complex arrangement found in man.

The so-called circulation of the blood was discovered very late in the history of man, and students have become so fascinated with the mechanical beauty of the whole arrangement that they have allowed the mechanical idea to outweigh the realization of a living organism. It is the old truth of the pendulum which has swung too far when once started by Harvey. We need to return a little to the earlier conception, which considered more the function of the blood in particular parts of the body than its circulation. In all studies of blood pressure it must be remembered that the blood is subject to the laws of hydrostatics and that the force of gravity must be discounted.

Anemia and Congestion.—In the study of the circulation in relation to disease, the two departures from normal that are most striking are anemia and congestion. But a moment's thought will show that these are not necessarily of as much importance as would appear. The other element, that is not so easily appreciable in the course of examination and upon which depends the efficiency of the blood supply, has very little to do with anemia or congestion. Anemia means that there is but little blood in the part under consideration, and congestion means that there is a considerable accumulation of blood in the vessels of the part. These two things are very striking symptoms of disease; and yet every clinical observer must have noticed that they are not reliable indications of disease.

The third element of local circulation in disease is the amount of new blood supply to the part which is the determining element in degeneration or repair. There may be apparent anemia, and yet what blood there is in the part may be constantly changed, and nutrition will not suffer. There may be marked congestion of the part, and yet the amount of fresh blood supplied and of impure blood removed may be sufficient.

This element is a very hard one to determine, even experimentally. The pulse itself does not indicate any transition of blood through the radial artery, because it persists, even when the artery is obstructed by pressure beyond where it is palpated and when no blood can pass. So, in an insufficient blood supply, or in an excess of blood supply, it is the amount of blood in circulation that is to be considered, and not the amount that is stored up in the part. In congestion without circulation, we find destruction of tissue, as in varicose ulcers of the leg. In congestion with circulation, we often find hypertrophy, as witness the clubbed fingers in chronic cardiopathy. In anemia without circulation, we again find that the nutrition suffers; but in anemia with circulation, there may be no disturbance of nutrition. In other words, the circulation of the blood may be compared to the circulation of the money in a bank. So long as the intake and outgo are active, the bank is going on all right, whether there is a large or small amount stored up in its vaults. Of course, in case of emergency, it makes a very great difference whether there is an accumulation or not. But under ordinary conditions, the outward signs of prosperity depend upon the in-go and out-take and not upon large orsmall accumulation. So, the importance of circulation is a question of movement of the blood, more than it is a question of particular location of that portion that is not in active circulation. Ordinarily, the part of the blood not in active circulation is found in the large veins of the abdomen, but it might just as well be in any other part of the venous system.

Estimation of Blood Pressure.—The estimation of the condition of the circulation usually represented by "feeling the pulse" stands for a very important procedure in the routine of the practice of medicine and is the one element of a physical examination that is probably never neglected. The tactile estimation of relative blood pressure, as determined by the experienced touch and checked by clinical symptoms, is often correct, and there is a possibility that some of this skill in pulse-reading may be lost if instrumental observation takes the place of direct examination, just as we have lost skill in measuring fever. However, the benefit following the introduction of instruments of precision far outbalances the resulting loss of skill. It is undoubtedly true that the systematic instrumental measurement of blood pressure by various instruments has led to important clinical results.

As remarked a moment ago, it is the difference in pressure between the place where the blood is stored and the place where it is required, together with the element of resistance in the intervening blood-vessels, that determines the competency of the circulation. The instruments and skill for the quantitative measurement of blood pressure, although brought to a high degree of perfection, are still not in the possession of the majority of practitioners. Our space here will not allow anything like a detailed description of the development of these various instruments. It will suffice for our purpose here merely to refer to such instruments as that of Professor von Brasch of Vienna who in 1876 invented what may justly be considered the first practical sphygmomanometer; his own and Potain's improvement a little later; Marey's instrument, with Hürthle's elaboration for measuring diastolic pressure; Mosso's complicated but highly efficient apparatus for the laboratory, and Hill and Burnard's "vest-pocket" instrument, whose chief merit is its compactness. But the very number of this class of instruments invented within the last two decades shows the importance of the subject of ac-

curate blood-pressure measurement. And this same prolificness insured such searching criticism of defects and struggle to overcome them that the perfected instruments of Riva-Rocci, Janeway, Stanton, and others may now fairly be considered practically to be instruments of precision.

In this country, the usual form of blood-pressure apparatus or sphygmomanometer is exemplified in that of the Faught apparatus, shown in the accompanying engraving.

It consists of a U-tube mercury manometer with a cuff to surround the arm and a rubber bulb to produce air pressure. For convenience in carrying,

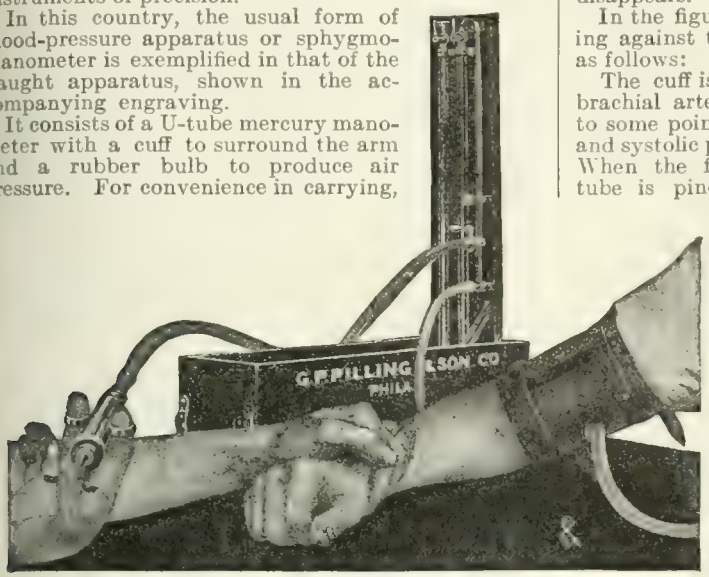

Fig. 811.—The Faught Sphygmomanometer.

there are various stopcocks to shut the tubes, and there is a release cock to release the air pressure.

Bishop's sphygmoscope is particularly useful for the detection of high-pressure and low-pressure cases in general practice and life insurance examination.

The instrument consists of the usual arm band, but pressure is made by fluid falling from a height through a rubber tube from a flexible rubber bag. The pressure is measured the same time that it is applied by regulating the height of the bag, and the pressure is read at the level of the brachial artery from figures placed on the tube.

The instrument consists essentially of an armlet fifteen centimeters wide and forty centimeters long, made of strong material. This armlet or cuff differs from the Riva-Rocci armlet in its greater width and in the fact that the rubber bag occupies only part instead of the whole circumference of the arm. The advantage of this latter arrangement is that the rubber bag when expanded compresses the artery against the bone rather than surrounds the whole arm which proved to be painful. Connected with the cuff is a red rubber tube.

Inserted in the tube near the cuff is a little glass arrangement, consisting of a tube with a lens blown on the surface of it. The lens is of such shape that its focus is at the center of the tube, and it magnifies the motion of any object in the tube in the direction of the length of the tube.

Inside of the tube there is a floating index. This index reveals any wave motion there may be in the fluid, the motion being magnified by the lens so that very slight waves are easily perceptible.

A special scale is attached to the bag at the level of its contents and is used to ascertain the blood pressure in millimeters of mercury. The instrument can be rolled up and carried in the pocket.

In use the arrangement is filled with a solution of 2,000 specific gravity. The bag is raised slowly until the pressure of fluid that has flowed back to the cuff has compressed the brachial artery and obliterated the pulse at the wrist. To find the exact point at which this takes place it is better to lower the bag until the pulse is distinctly felt again, and then raise it two inches at a time, counting ten beats of the pulse each time until the pulse disappears.

In the figure, the sphygmomanometer is seen resting against the shoulder of the patient. It is used as follows:

The cuff is laced on the arm with the bag over the brachial artery; then the reservoir bag is elevated to some point that is probably between the diastolic and systolic pressure, for instance, 100 in most people. When the fluid has reached an equilibrium, the tube is pinched below the reservoir, and immediately a pulsation is visible in the sphygmoscope, corresponding to the pulse in the brachial artery. The reservoir is now lowered a little bit, and the tube again pinched and the pulsation observed. This is repeated until a point is reached where the pulsation becomes suddenly and markedly diminished. This is the diastolic pressure, being, according to Marey's criterion, the lowest point at which the maximum pulsation is conveyed from the artery to the compressing medium. Systolic pressure is determined by the point of disappearance of the pulse.

The inventor has tested this instrument with all kinds of cases and compared them with the standard instruments, and has found that its readings are correct. He finds that a closer reading is often possible with this instrument than with the other instruments on account of the absence of fluctuations and greater length of the scale. This is especially true in low-pressure cases and very high-pressure cases. The instrument is particularly convenient for detecting cases that fall into his classification of blood-pressure cases, namely,

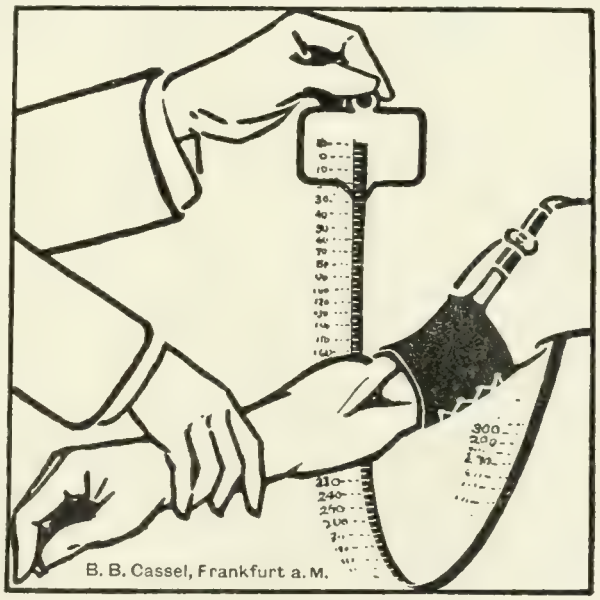

Fig. 812.—Bishop's Sphygmoscope.

primary low-pressure cases, high-pressure cases, and secondary low-pressure cases.

Another form of instrument in much use is the Tycos sphygmomanometer. An aneroid manometer is employed, and it is used the same as other instruments, as shown in Fig. 813.

Symptomatology.—The symptoms of disorders of blood pressure divide themselves into subjective and objective groups.

The subjective symptoms depend upon the influence of circulation upon the sensory nervous system, and upon the appreciation by the individual of the local changes in the blood supply. Among the organs of the circulation are the brain and the kidneys. The brain is a highly sensitive organ, the most striking function of which is consciousness. The kidneys are insensitive organs. The brain is the most prominent organ of conscious circulatory symptoms, and the kidneys the most prominent organs of those symptoms of circulatory disease that develop gradually and insidiously. Changes in the peripheral circulation often go on simultaneously, producing evidently conscious symptoms, referred to the brain, which lead the physician to seek evidence of disease in the kidneys. Owing to the control of the circulation largely exercised by the nervous system, it is natural that the most striking changes in the blood supply are often found in nervous disease. In hysteria, neurasthenia, and other so-called functional nervous diseases, the vasomotor system becomes disturbed, so as to lead to the most erratic distribution of the blood. In true insanity of maniacal type, high blood pressure is very common; and in depressed types, poor circulation, with cyanosis of the extremities, is most characteristic. From all this, it may be inferred that the symptomatology of disorders of the blood-vessels needs to be analyzed to separate the signs of important organic conditions from those that are not essentially due to disease of the blood-vessels, but are the temporary expression in the circulation of other conditions. In deciding this, the measurement of blood pressure in the arteries is of the greatest importance, because the persistent rise of blood pressure is an indication of circulatory disease, present or to be developed.

The direct examination of the radial artery for the detection of disease of the vessel itself is the first step in diagnosis of arterial sclerosis. Palpation of the radial artery, as represented by feeling the pulse, is the one element of physical examination that is never neglected by any physician in any case of illness. Hence, it represents an unusual degree of experience. Arteriosclerosis is often detectable by the examination of the pulse, or rather of the radial artery and its pulsations. The artery is to be examined with the tips of all the fingers; first studying the pulse-wave, then the amount of pressure necessary to check these pulse-waves. Then the attention must be turned to the artery itself, which must be examined for patches of atheroma; not because atheroma and arteriosclerosis are the same condition, but because atheroma is very apt to be present in arteriosclerosis.

Diagnosis.—The diagnosis of circulatory disease depends first upon the recognition of disorders of the blood-vessels, and then upon the decision of the question whether these symptoms are merely due to the natural disturbance of the circulation incident to some other disease, or whether the condition is essentially a disorder of the circulation itself. But some other disease may originally cause the circulatory trouble, and the latter may persist after the other disease has come to an end, or outbalance it in importance.

When disease of the blood-vessels is suspected, the symptoms to be elicited in the interrogation of the patient are first those that the patient connects with circulatory disease and those that pertain to our own knowledge of the effects of disturbed blood supply. The ordinary symptoms of vasomotor disturbance are chiefly observed in the skin. Dilatation of the blood-vessels is accompanied by sensations of heat, throbbing, and perhaps sweating. This vasomotor paralysis will be found most commonly with nervous symptoms, but frequently occurs as an independent affection. Or, on the other hand, in a case of vasomotor spasm, there are striking pallor and coolness of the skin, with a feeling of itching and often great discomfort. This is most frequently observed in the hands. Sometimes the patient will be conscious of heat and redness of one part of the body, while another part is cold and pale. Vasomotor disturbance may be so great as to give rise to local swelling, due to the effusion of serum, or even to gangrene due to vasomotor spasm.

Fig. 813.—Rogers' Tycos Aneroid Sphygmomanometer.

The symptoms of circulatory failure are not alone dyspnea, edema, and visible congestion or anemia, though these are the cardinal indications. There are certain symptoms of obscure origin traceable to circulatory disease, which are overcome only when that is given proper attention.

In elderly people, one of the most frequent and troublesome of symptoms is that of head noises. I have under observation at the present time no less than four patients who have suffered over long periods of time from noises referred to the ear, which they described as puffing or blowing sounds, and which have been extremely annoying. These patients had all been systematically and heroically treated for ear disease without benefit; but when the circulation was properly controlled, the noises become so slight as not

to be complained of, and a good deal of the time not to be noticed. These patients are usually found in the group of commencing secondary low arterial tension. The explanation of these sounds would seem to be the circulation of blood through badly filled blood-vessels in the neighborhood of the organ of hearing. There is no class of cases the treatment of which has given greater satisfaction, because it is possible to relieve the condition that causes so much suffering particularly at night.

Another obscure manifestation of circulatory disorder is the simulation of slight attacks of paralysis. These are often overlooked unless they are watched for. They consist of a temporary slight loss of power of a transient nature, on one or the other side of the body. The patient usually describes the attack as a "clumsiness" of a leg or an arm. If on the right side of the body, there is sometimes a slight loss of power of speech, in that certain words are missing. The patient usually considers this a temporary failure of memory. These manifestations are often the same as those which indicate more serious disease of the brain with impending thrombosis. However, in many cases, attention to the general circulation will entirely remove the symptoms, so that it is hard to believe that the condition was purely local in origin.

There is a class of obscure symptoms of circulatory disorder which consists of pain in various parts of the body. How much of this is purely circulatory and how much of it belongs to the gouty, rheumatic, and nutritional disorders that are common in the same class of patients, is often hard to determine. It is suggestive that these painful conditions arise at times of circulatory debility and improve when the circulatory disease is in abeyance. Attacks of sciatica of a persistent and troublesome nature are particularly apt to occur in patients commencing to suffer from secondary low arterial tension.

There is a really pitiable class of patients who may be mentioned here, though perhaps not quite logically. These are persons who have developed a very painful and chronic neuritis subsequent to attacks of extreme circulatory edema of the lower extremities. It may be only a coincidence, but this has been among the most difficult conditions to relieve of all that have come under observation in connection with the treatment of circulatory disease.

The description of obscure symptoms of circulatory disease would not be complete without a consideration of those that may happen during the stage of high arterial tension. Nosebleed of a troublesome character is a frequent occurrence; and in cases in which one is puzzled to decide between primary and secondary low arterial tension the history of a period during which nosebleed was very troublesome may be of help. It is surprising how often this history is elicited from patients who come for the first time in the stage of broken compensation.

The number of conditions due to congestion secondary to general circulatory disease that are mistaken for diseases of local origin is very great. The most striking of these is, perhaps, congestion of the liver. This develops gradually, the blood collecting in the liver and giving rise to functional derangements of this organ and of the other organs of digestion. The liver is enlarged and tender on pressure, and the condition is often accompanied by very marked disorder of the stomach, on account of which it is frequently mistaken for primary gastric disease. That this is not the case is proven by the fact that the condition is relieved only when the circulation is strengthened.

The circulatory disorder may also be shown in its pulmonary effects. There is persistent congestion of the lungs, often with a tendency to the accumulation of serum in one or both pleural cavities. These patients may often have a fairly good systemic circulation and very obscure indications of cardiac disease. The interference is apparently with the function of the right side of the heart. Two patients of this character were watched over a long period of time, while the pulmonary congestion, involving repeated attacks of bronchitis and slight edema, rendered them incapable of work. The circulatory disorder is masked because the symptoms are so much more accentuated in the thoracic organs than elsewhere.

Circulatory disorder may also show itself in its effect upon the function of the brain by attacks of acute mania, or more often by the development of a chronic mania. Changes in the arteries in elderly people are apt to be characterized by changes in disposition, by affections of the memory, and by impairment of judgment. The circulatory derangement may be shown by so striking a manifestation as general convulsions. These patients are often supposed to be suffering from idiopathic epilepsy. However, the attacks are so promptly relieved by appropriate treatment directed to the circulation, which would have no effect whatever in epilepsy, that this may be eliminated from the diagnosis. Of course, there are relatively rare cases in which real epilepsy begins late in life.

A group of symptoms on the border line between neurotic and circulatory disturbances forms in its sum total a large proportion of the sufferings of humanity. Abnormal sensations in the extremities, numbness and tingling of the hands and feet, a feeling of formication extending up the legs and thighs, abnormal coldness of the hands and feet, cramps in the muscles of the legs occurring at night, and the tendency of the extremities to "go to sleep" as it is called—all these things may be pure neuroses, but often enough there is a circulatory element in their causation. As was suggested in a preceding paragraph, we may again remark that the therapeutic test will decide how much of this is due to disorder of the circulation. Many times the symptoms disappear when the circulation is properly regulated. A few doses of nitroglycerin have stopped all complaint of cold extremities in many patients of this type. The possible severity of pain due to interference with the circulation is well shown in cases of embolism of the extremities in the course of circulatory disease. No one who has observed this accident will doubt that pain of the severest type may be due to interference with the circulation.

High-tension and Low-tension Cases.—There are two great groups of high-tenson and low-tension cases and a third group of secondary low tension following high tension.

Primary Low-pressure Cases.—Disorders of the general circulation are generally first recognized when some particular portion of the body becomes the seat of a marked congestion or anemia. Then two conditions often produce symptoms that are strikingly similar. Delirium may be the result of congestion of the brain, but it may likewise result from anemia. Dyspnea may be an accompaniment of congestion of the lungs, but a deficient blood supply is its most common cause. Acute congestion of the kidneys causes suppression of urine, while diminished blood supply causes deficiency of secretion.

The effect upon an organ is a matter of the proper supply of fresh blood, not merely of a greater or lesser amount of blood in the vessels of the organ. This explains beautifully the effect of local therapeutics, such as the removal of a small quantity of blood, or the institution of some form of counter-irritation, the result of which is to start up a stagnant local circulation. There is, however, little gain from the treatment of local congestion or anemia without attention to the general circulation in cases where the cause is general. Hence the extreme importance of recognizing which cases are of purely local origin and which have their origin from the general circulation.

During the acute stage of valvular disease, in the

large majority of cases, circulatory failure does not become a matter of special anxiety. Low arterial tension usually shows itself when the patient resumes his ordinary occupation. The symptoms are practically the same for all forms of valvular lesions, although different in degree. The important question is whether the defect has been properly compensated, and whether this compensation can be maintained. In general, however, it may be considered that in aortic disease the defective circulation is more strikingly due to an insufficient supply of blood in the arteries, and in mitral disease to an increased pressure in the veins, both resulting in a diminution of the difference in pressure in the arteries and veins, upon which the proper passage of the blood through the tissues depends.

The belief, so firmly held by many, that cardiac disease is usually confined to the left side of the heart is not borne out in practice. The most serious and fatal disorders involve the right side of the heart. It is true that inflammation and distortion of the valves are almost entirely confined to the left side of the heart, but it is likewise true that both sides suffer equally in the incompetencies of the valves that come from strain or weakness of the heart muscle, as seen in very many cases of disorder of the circulation. The left side of the heart can be markedly deficient in mechanical detail or physical structure and the patient may get along fairly well until dilatation involving the right side of the heart takes place with tricuspid regurgitation and its resulting venous engorgement.

Low arterial pressure is to be regarded as pathological only when it is so little above venous pressure that the tissues and organs are not properly supplied with blood. There are instances in which the heart is perfectly able and willing to produce more arterial pressure, but the peripheral circulation is so relaxed that it is not needed. We get dangerous low-pressure cases when the pressure-producing mechanism has failed. These are primary when there has not been a previous overdemand for pressure. Low blood pressure due to general prostration is not to be regarded as a disorder of the circulation except in so far as the circulation fails to respond to demands made upon it. Thus in shock it is the nervous system that is at fault, not the circulatory apparatus.

The indications for treatment in disorder of the circulation characterized by deficiency in pressure in the blood-vessels, which is primary in that it has not been preceded by high arterial tension, are simple, though the elaboration of the management of each case will tax the judgment and ingenuity of the physician. When there is no defect in the valves and no tendency to obstruction in the arteries the condition is usually a weakness of the heart, and much may be accomplished by iron, arsenic, and hypernutrition, by increasing the number of meals, and by outdoor exercise.

In the early days of a newly acquired valvular lesion, prolonged rest in bed with the very gradual resumption of a more active life will enable both the heart and the body in general to adapt themselves to the new conditions. Of necessity, there must be a compensatory hypertrophy, but it is not to the advantage of the patient that the hypertrophy be excessive, hence the desirability of such gradual resumption of active work. Until subjective symptoms and objective signs of defective circulation have disappeared, the patient must be restricted to a very quiet existence. The use of drugs at this time is usually inadvisable, yet in cases of long-delayed compensation digitalis may be used.

When compensation is established and proper pressure in the arteries maintained, these cases may still be classed in the category of low arterial tension because of their tendency to this condition, just as we consider cases of Bright's disease as being high-pressure cases, even when the condition is not actually present at the time.

During the stage of compensation, which may be of long duration, the patient should lead a well-regulated existence—physical overexertion, mental overanxiety, and dissipation of all kinds must be avoided. The occasional use, during the stage of compensation, of the iodide of sodium as a means of preventing degeneration of the hypertrophied heart is a useful procedure even when no other drug therapy seems advisable.

In the progress of cardiac disease there are many elements that are not unlike the advance of tuberculosis. The term "cardiac cachexia" has been applied to a form of this condition accompanied by congestion, but it might well be extended to include the deterioration of fiber which leads to failure of the circulatory apparatus. In tuberculosis, the connection between the cachexia and the disease is so evident that its hygienic management needs no advocate. It is equally true that the progress of circulatory disturbances is often dependent upon nutritional causes, and that the hygiene of tuberculosis in its demand for fresh air is equally important to the cardiac patient. The vitalizing effect of fresh air in these cases will more than counterbalance the dangers of catching cold, although care is necessary when inflammation or congestion of the kidneys is present. The patient can be trained to sleep with open windows.

Low pressure due to degeneration of the heart muscle which has not been preceded by hypertrophy is not at all common except in connection with acute or chronic general disease. But little is accomplished by measures directly influencing the circulation. The same is true of the heart overloaded with fat. Treatment must be hygienic, though the defective heart muscle demands precautions.

High-pressure Cases.—By high-pressure cases are meant those circulatory disorders which are characterized by undue resistance in the circulatory path of the blood. It is not necessary, for cases to be classed in this category, that actual high pressure should always be present in the blood-vessels. High-pressure cases comprise all instances in which degenerative disease of the blood-vessels or kidneys, brain tension, or toxemia causing disordered action of the same and resulting in high arterial tension, precedes or goes hand-in-hand with the development of cardiac disease.

Low-pressure cases occasionally become high-pressure cases, as when valvular disease of the heart causes secondary Bright's disease.

The management of high-pressure cases, which include a large proportion of the slowly developed diseases incident to the overwork and luxury of modern times, is relatively more important than that of the low-pressure cases. It is particularly important to detect the earliest development of a tendency to high arterial tension, because at this time it is more amenable to treatment.

As implied above, in this class of cases the heart, blood-vessels, and kidneys go hand-in-hand, and serious disease of one is not found without involvement of the others. Hence the term "chronic Bright's disease" is frequently used in speaking of these cases. But chronic Bright's disease is not essentially a disease of the kidneys, although in the final catastrophe these organs are often chiefly at fault. Primarily, it is a disease of the circulation in which the brain and kidneys, acting as it were as end-organs, first manifest symptoms.

A case which had been under observation for five years ended fatally by the involvement of the circulation of the brain, producing progressive stupor, and finally coma, paralysis, and death. The kidneys at the time were apparently in good enough condition to have functioned fairly well for a much longer time. In this case, the greatest care had been exercised in

protecting the kidneys by diet, an even temperature, and every other possible means, thus allowing the arterial disease an opportunity for its complete development. The same case, if less carefully guarded, would have progressed, by repeated attacks of uremia, to a death by the development of anasarca and exhaustion. We have, then, the paradox that a person may die from Bright's disease with fairly good kidneys.

This point is important in considering the early symptoms in high-pressure cases. The kidneys are insensitive organs, rarely giving rise to pain, intermittent in their manifestations, and entirely removed from direct observation; for this reason disorder of the kidneys may reach a grave stage before it becomes a matter of consciousness. On the other hand, the brain, as the seat of consciousness, is highly sensitive to any interference with its functions. To a certain extent its circulation is capable of examination through the observation of the fundus of the eye, which is in close relationship to the brain.

Even in cases in which chronic Bright's disease follows acute nephritis, one watches the circulatory system with anxiety, because, when changes are established, the chance of complete recovery is diminished. In acute Bright's disease the heart is temporarily debilitated so that there is often established a blowing systolic murmur at the apex, and the profound anemia and nervous phenomena that accompany the disease may lead to other functional disturbances of the circulation. These must, however, be distinguished from the changes that take place in the arteries which indicate the transition from subacute nephritis to the chronic general condition. The same change sometimes indicates the establishment of a chronic nephritis in cases of valvular disease of the heart that have been accompanied by prolonged congestion of the kidneys.

Cardiac hypertrophy is often the earliest detectable sign of chronic nephritis. Abnormal arterial tension may for the moment be absent, either on account of treatment or from some other cause; but when physical examination shows distinct cardiac hypertrophy, we suspect at once a high-pressure case of circulatory disease.

It is probable that an increased flow of urine found in early Bright's disease is due as much to increased blood pressure as to any definite change in the kidneys. Nosebleed is another possible result of increased arterial tension, and may therefore indicate the beginning of Bright's disease. Another accompaniment of increased arterial tension is headache, due apparently to increased vascular tension in the head. I would also mention, as one of the early disturbances of high-pressure cases, attacks of indigestion. These are due at this early stage to disturbances of circulation in the stomach, and are not to be confounded with uremic nausea.

High-pressure cases more often develop in an atypical than in a typical way, and even in their final fatal course may never present the symptoms that one would expect. The early symptoms are often an unhealthy look, loss of strength, and such disturbances of digestion as may be referred to simple weakness. The urine may contain albumin only at rare intervals, so that it may not be detected by anything save systematic observation.

It is fair to say that the early signs of impending changes in the blood-vessels also mean the early circulatory changes of Bright's disease. The first signs of degeneration are manifested by disorder of function. The blood-vessels act as tubes to convey the blood to different parts of the body as it may be most needed. It is this regulating function which first suffers when the tendency to high pressure begins to show itself, so that irregularity of tension is the most important early circulatory indication. The smaller arteries are attacked earliest, and these are the first to show disordered function. Increased arterial tension, or a tendency to it, causes irregularity of blood pressure, and is early recognized by symptoms indicating irregularities of circulation in particular parts of the brain. This irregularity may give rise to temporary unconsciousness, slight paralysis, or simply to clumsiness of a limb.

The typical high-pressure case, as met with in practical work, is usually one which has gone on to its full development without observation or treatment. The patient presents himself because he has symptoms, or because on some occasion an examination has revealed the chemical or physical signs of the condition. The heart is found hypertrophied, the arterial tension high, and the urine increased. Careful questioning will elicit symptoms of disorder of the cerebral circulation as indicated by a subjective feeling of nervousness, headache, insomnia, or attacks of dizziness, or even threatened aphasia and hemiplegia.

The Blood-vessel Tone-maintaining Function of the Brain.—As we trace the development of the circulation from the lower forms of life up through the scale, we find that the control moves closer and closer to the central nervous system. In the higher forms of animals a tone-maintaining function is easily traced to the medulla, and I believe that, in man at least, an important part of this function is found in the cerebral hemispheres.

It is well-known that there is a tone-maintaining influence originating in the motor areas of the brain that preside over the tonicity of the voluntary muscles. When a stroke of paralysis occurs, due to damage to the part of the brain that presides over the motion of a limb, that limb is paralyzed with regard to voluntary motion, but at the same time there occurs a relaxation, a loss of tone, in the blood-vessels that causes swelling. This suggests the fact that the involuntary muscles were likewise involved in a loss of tone, and would seem strong evidence of this blood-vessel tone-maintaining function. Not only may local blood-vessel tone be affected by changes that occur in the brain, but also the general tonicity of the whole circulatory system. In all brain conditions, we look for changes in the peripheral circulation. Emotion may cause a rapid rise of blood pressure. It is said insane asylums are full of high-pressure cases due to cerebral excitement. In cerebral neurasthenia the blood pressure is apt to be low.

In advocating the recognition of a blood-vessel tone-maintaining function of the brain it is not necessary to minimize the importance of the center in the medulla, whose activities in this direction are so well known. It is only necessary to believe that the activity of this center is dependent upon stimulation received from the brain. A recognition of this function of the brain, which exercises a general control over vessel tone and therefore over blood pressure, makes it much easier to understand many important disorders of the circulation; and the benefits of certain plans of treatment which experience has proved to be of the greatest value. It explains why exercise of the voluntary muscles has so good an influence over disorders of tone of the involuntary muscles. It makes clear why resistance exercises have vindicated their right to a place in the treatment of disease of the heart. It also reveals the development and points the way to treatment of idiopathic vascular hypertension, a disease the importance of which is becoming more and more recognized every day.

Hypertonia Vasorum Idiopathica.—This is *par excellence* the disease of the present day and is looming up as of more and more importance in proportion as it is better understood. The time cannot be remembered when successful men were not stricken down in the midst of their activities by apoplexy or so-called heart failure, but of late years it is increasingly com-

mon for those men and women who play the most prominent part in the world and carry the heaviest burden of responsibility, to develop finally disorders of the arteries of the brain or of other vital organs, resulting on the one hand in apoplexy or on the other in Bright's disease. We have attributed these breakdowns too often to chemical causes arising from disorders of the digestive system, or we have regarded them as primarily disease of the kidney, developing in some mysterious way. Too often has alcohol been blamed when in reality it was hardly a factor in the case. Why should it be that persons preeminent for the use of their brains, and singled out for the heaviest responsibilities, suffer in the direction of the circulation so much more than those whose occupation is of another character? The reason is to be found in the effect of mental strain in exaggerating that tone-maintaining function of the brain that was discussed in the previous section.

Let us trace the development of such a case, resulting in an attack of apoplexy. A composite picture, drawn from the mental concept of this disease, tallies almost line by line with many concrete examples. The patient is a man of good family history, inheriting sturdy qualities from an ancestry that has developed strength through the successful contest with the difficulties of the development of a new country. He has been well educated and has led a healthy and active youth. From the very beginning, he has been a worker among his fellows and, spurred on by one success after another, by middle life he has attained a position of importance and usefulness. Now his qualities have been recognized, and one burden after another has been laid upon him. He has become a factor in government, in business, in intellectual pursuits, and in philanthropy. Such a man, unmindful of the fact that he is past middle age, and that the body no longer has the recuperative power of youth, continues his work unceasingly, without those relaxations that attract men of a lighter turn of mind. The man feels perfectly well, but a change has taken place in the machinery of his body. The influence from the central nervous system, which maintains the blood-vessels in a proper state of tonicity, has become exaggerated through the overflowing of the mind strain, and the blood no longer circulates with ease. Now it is hard to keep the blood in proper circulation, but without any manifest symptoms the heart becomes enlarged and still carries on the work. The two factors of arterial contraction and cardiac hyperactivity result in high blood pressure. This in turn results in structural damage to the blood-vessels in the brain, the kidneys, and elsewhere. Unconsciously, the man is living in constant danger. Some day there arises some incident in his career that leads to an unusual degree of worry or mental strain, and there develops a tendency to inflammation in the already damaged blood-vessels of the brain, the blood clots the circulation, most likely near the speech center on the left side, and another prominent man has fallen victim to an attack of apoplexy. Sometimes the picture is varied and one of the arteries that supply the heart substance with blood is stopped, and the man drops dead in his tracks; or in another case the kidneys gradually give out. Not infrequently the abdominal arteries show the first indications by terrific digestive disturbance, causing great distention of the stomach with gas and marked irregularity of the heart. This is my mental concept of hypertonia vasorum.

Even after any one of these serious accidents, much can be done for a man made of such good stuff, but how much more satisfactory would be the prevention of such an accident by proper medical treatment and a suitable regimen!

I would register a protest against those who decry the use of drugs in circulatory disease, because in all medicine there is no condition in which proper drug treatment is of greater value, and none in which, to my mind, its usefulness seems more easily demonstrated. The remedies must, however, be used with appreciation of the fact that that they are to regulate an active mechanism that is always changing in its demands, and that the one needed at one time may be contraindicated a little later.

This implies very careful medical supervision, particularly when the case first comes under treatment. By a process of re-education of physiological processes, control of function becomes easier and easier; and, as the patient becomes familiar with his tendencies, the physician can in a measure yield control. The details of treatment must be worked out for each individual with due regard to the relation of blood pressure, heart disease, and blood-vessel damage.

The management of high-pressure cases is perhaps the most important part of our subject, as it is also the one in which the greatest advance has been made. The recognition of the functional element in cardiovascular disease marks perhaps the greatest single advance in the appreciation of the therapeutic needs of patients suffering from disorders of the heart and circulation. If we believe that the therapeutic modification of function is of advantage only so long as the effect of our remedies lasts, then we must indeed be therapeutic nihilists, for truly enough we cannot continue indefinitely to use vasodilators, cardiac stimulants, and alteratives. We have faith in the cure of cardiovascular disease because the persistent and patient modification of function by diet, drugs, suitable exercise, and a carefully selected environment finally educates the person's physiological activities so that they act normally after the withdrawal of active measures. This education or re-education, by which functional derangements are removed, holds out hope of a permanent cure of hypertonia vasorum and the removal of damaging high blood pressure. It is, of course, most useful before tissue damage has been wrought by the pressure violence to the nutritive vessels of the heart, brain, or kidneys.

In an early case of high arterial tension of nervous origin the important element in physiological re-education consists in training the victim to eliminate worry and a tendency to too great concentration of interest in whatever pursuit is occupying him. Worry is in a measure a habit and can be eliminated by a person of strong intellect, who definitely decides to let events in a measure take their own course, and the too great concentration on one's occupation is a self-indulgence that often ignores the importance of other things and the legitimate claim of the lighter things of life upon the attention.

The business man should be content with a reasonable financial success, and the professional man with a reasonable degree of distinction. In a paper read before the New York State Medical Society in 1907, Dr. H. L. Elsner pointed out that physicians themselves should be on their guard lest they suffer from the evils of high tension in their own circulation. The patient should deliberately eliminate under the advice of his physician all unnecessary burdens of responsibility. If the man or woman has occupied a position of trust, and has given that devotion to work that has led to hypertonia in the circulation, he or she is certainly entitled to pass the burden on to some one else. Often enough, when unnecessary burdens are thrown off, it is perfectly possible to take care of what are left. The world is not to be reformed in one generation, and no one was ever meant to carry the burdens of the universe.

Next to the elimination of worry and undue concentration of mental effort comes the question of nutrition and diet. Many persons consider themselves undernourished, when in fact the opposite is the case. A critical examination of the blood and urine often shows distinct evidence of an excess of food in persons who are seeking to be built up by physical rest and a

diet selected for its nutritious qualities. When this is the case, the food should be restricted in quantity—sweets eliminated, and meat greatly reduced. The popular prescription of withholding from these patients all food that has contained blood may be extreme, but it is in the right direction. Third, but not least in importance, is the matter of physical exercise. Here we come upon the relationship, which I have often traced, between the tone-maintaining function over the voluntary muscles, and a possible similar function with regard to the involuntary muscles. Exercise should be carried on systematically, whether the patient feels like it or not. A distaste for physical exercise often goes with this condition, and must be overcome by emphatic instructions by those responsible for the welfare of the patient. There is, undoubtedly, some advantage in the resistance movements, though massage does not seem suited to many patients with high blood pressure. It has seemed to me that the resistance movements were valuable in removing overtone through some connection with the tonus of the voluntary muscle. While the patient is under treatment, or re-education, the circulation must be regulated as far as possible by drugs that improve the muscular tone of the heart and those that overcome an excess of tone in the blood-vessels. These must be given under skilled direction of some one who has the knowledge and authority to regulate the time, quantity, and nature of the medication almost from hour to hour, to meet the manifestations of the pathological physiology of the disordered circulatory system. In some instances a few weeks will counteract the commencing high tension, and the individual may go on for years without its developing again. In more severe cases, several months are necessary. In cases that have lasted a long time a year is necessary for the physiological re-education. The intelligent coöperation of the patient and the friends of the patient is absolutely necessary. In difficult cases, the work is most discouraging at first, though often enough after a few weeks the beneficial results become rather suddenly apparent to every one. Where there are distinct evidences of broken compensation, treatment must, of course, be commenced by keeping the patient in bed, but these patients can often least afford the debilitating effect of bed treatment, and the sooner outdoor treatment can be instituted the better. An attack of apoplexy does not preclude the possibility of good results from physiological education in high-pressure cases, but, of course, makes the problem more difficult. Particularly is this true when, as is often the case, there is a distinct tendency to depression of spirits, approaching melancholia; for the mental tension that goes with this stage makes the high vascular tension hard to control. Physiological re-education should begin early, but unfortunately this newly recognized condition of idiopathic vascular overtone is not generally enough recognized for the necessity of such active treatment to be appreciated as often as it should be.

In its early stages it is a disease without symptoms because the heart first brings into play its reserve force, and then painlessly becomes enlarged, and the severer accidents of the development of Bright's disease, of apoplexy, or of heart failure have to do only with the fully developed condition. It behooves every one, particularly if over fifty, to have the vital organs inspected at regular intervals, so that overtone may be early recognized and prevented.

The Use of Nitrites.—When Brunton applied amyl nitrite to the treatment of angina pectoris, he achieved a signal triumph in therapeutics. No less was the triumph of the more gradual application of the nitrites in general to the treatment of vascular spasm. These were first well used by those who had witnessed their development and were familiar with their philosophy and limitations. Unfortunately, the student, coming later upon the field of medicine and finding the nitrites in general use for vascular disease, jumped naturally to the conclusion that they were the remedies *par excellence* and used them in a routine way in the treatment of these cases. The observation of this fact makes it seem useful at this time to emphasize the necessity of conservatism in this matter. It is a trite saying that we should always treat the patient and not the disease, meaning by this that we must carefully recognize the exact physiological and pathological conditions present, and so influence them as to bring about the cure of disease. Patients differ widely in their behavior under the nitrites, and for that reason every case requires physiological study to determine the amount of drug necessary and how it should be applied. To apply vasodilators without also instituting hygienic measures to reduce the irritability of the heart and restore the exhausted or disordered nervous system is to overlook an important element in the problem of cure. The necessity for the use of vasodilators is diminished in proportion to the intelligence and success attending these accessory measures.

In Bright's disease there is probably some substance circulating in the blood that irritates the muscular coats of the vessels and causes contraction. This, with the physiological attempt of the heart to carry on the circulation, again brings about high tension. When high tension antedates the onset of nephritis it may well be supposed that the tension has something to do with the production of nephritis.

A physiological increase of blood pressure is caused whenever there is nervous, muscular, or physiological exertion. Prolonged nervous strain, such as that met with in an exciting business career, or in prolonged dissipation, keeps up a tendency to tension that is particularly apt to lead to arterial degeneration. Muscular action is less prone to produce damage, and probably does so only in rare instances of long training and severe contests of strength. The reason for this is that exercise is accompanied by natural dilatation of the arterial circulation, improved nutrition, and relief afforded by perspiration. The physiological activities of the body are usually accompanied by too slight a stimulation of the circulation to count for much in health, but are worth considering in disease.

In the case of a person suffering from abnormal tension, it is especially important to do away with mental strain and responsibility. Such a person should not indulge in violent exercise, but is benefited by slow exercise. Food should be moderate in amount, taken at frequent intervals. A study of each individual should be made and a few-proteins diet adopted, such proteins as the patient is found to have suffered from being excluded.

When the vasodilators are given it is to produce a definite physiological effect which is capable of being appreciated by the observer. The dose required to produce this effect differs widely in different individuals and under different circumstances. In a large number of cases the remedies are now so given that no effect whatever is produced. Crude therapeutic thought is responsible for this. The idea is conceived that the nitrites are good for kidney and heart disease, and so they are administered with the hope that the patient may be benefited thereby. If improvement takes place the medicine receives the credit, whether it has done its work or not. The word "conservatism" means more than caution, more than small dosage. It means the working out of the possibilities of the remedy and its application in such a way as to fulfil its broadest mission, so that it may not be wasted or abused—wasted when used in non-active doses and abused when used too often or in too great quantity. With the vasodilators a careful regulation of the dose is of vital importance, for their final action may be dilatation and paralysis of the heart through a complete breaking down of that great power which moderates all muscular activity.

When nitrites are used it is also of the utmost

importance that the preparation selected should be reliable. I have known patients to take for a long time tablets supposed to be nitroglycerin which were frequently found to be inert. When no benefit is obtained in conditions in which nitroglycerin is clearly indicated, this may be fairly suspected. As a test, one of the tablets should be given to a healthy person, who should immediately feel the throbbing in his head due to the dilated blood-vessels and the stimulation of the heart. If no effect is felt, a new preparation must be sought and this tested. The one-per-cent. solution of glonoin is probably more reliable, but is not nearly so convenient for patients as the tablet. I have found granules of nitroglycerin, gr. $\frac{1}{225}$, very convenient.

Cases must be studied from time to time by the withdrawal of these drugs, and by the substitution of other drugs of a different class. Particularly is it important in every such case to know from actual observation the effect of digitalis in such doses as bring about distinct physiological phenomena.

But few diseases can be treated by specific measures, and cardiovascular disease is particularly remote from such an ideal. The end which drugs accomplish is such control of the circulation as will tend to benefit the condition of the tissues, or the prevention of the condition of these tissues from working injury to the body as a whole. The management of cardiovascular disease is like the running of an intricate machine. The physician must study the machine itself and learn all its resources. He must know the use of every tool and the effect of the turning of each screw. It is no abuse of the privileges of the physician to study his cases therapeutically by testing from time to time the effect of different classes of drugs, though he return after each trial to the original plan of treatment. It is the height of arrogance to assume that his inductive reasoning can plan for each case a permanent course of management. Such action would lead only to humiliation and disappointment. How exasperating it is, when for a long period of time, on theoretical grounds, we have abstained from the use of such a drug as digitalis, to find, some time or other, that our patient has taken it through the advice of the corner druggist and has received appreciable benefit from it! Of course, we know very well that the corner druggist had no right to experiment, but perhaps the risk was worth taking, after all.

There is a particular form of pulse in which nitroglycerin is not so valuable as a number of other drugs. This is a high-tension pulse, with persistently rapid heart action. In these cases, I have sometimes seen the greatest benefit from the use of digitalis. Nitroglycerin has a twofold action in stimulating the heart and dilating the blood-vessels. Digitalis has a twofold action in slowing the heart and contracting the blood-vessels. Theoretically digitalis would not act in these cases; but practically in a case of nephritis with a high tension and rapid pulse, digitalis will often show its controlling action upon the heart in greater degree than any of its other effects, and in that way bring about a slower pulse with less apparent tension. At the same time, digitalis will clear up congestion of the kidneys and cause a better secretion of urine.

Even when tension does exist in cardiovascular disease with nephritis, it should be realized that some tension may be desirable. As time goes on in such a case, the greatest danger to be feared is a too great lowering of the blood tension, with its accompanying congestions and effusions. In the presence of symptoms indicating disturbances of cerebral circulation, such as numbness or awkwardness of one of the extremities or slight difficulty in speech, the vasodilators are imperatively needed. Sodium iodide has also an undoubted power to postpone paralytic attacks due to the plugging of blood-vessels.

A word as to the possibility of recovery from cardiovascular degenerative disease. The heart symptoms are those of myocarditis and the kidney symptoms those of chronic nephritis. The tendency of the blood is to become of poor quality. Every one knows that under ordinary circumstances a person starting with this form of disease has a tendency to become worse. However, I do not believe that this need always be the case. With a properly planned regimen and the possibility of carrying it out, and with careful medication and other therapeutic measures, the heart may recover its tone so that all symptoms of degeneration will disappear, and the kidneys may settle down to do their work according to a particular plan, but well enough for the maintenance of health.

It is hard to prove the regeneration of kidney tissue, though the physiological hypertrophy of one kidney when the other is removed leads to a belief in its possibility. Certainly there are many persons passing a large quantity of urine of low specific gravity and with a slight trace of albumin, who maintain year in and year out signs of health. Their heart, blood-vessels, and kidneys have readjusted themselves and, though bearing the scars of disease, are carrying on the functions of the body in a satisfactory manner. I have pictured this condition because it is extremely interesting to decide in these cases how much we should intervene with drugs to alter the heart action or relax the blood-vessels. It seems to me that in the absence of symptoms sodium iodide will accomplish the best purpose and that the use of the nitrites should be limited.

Management of Secondary Low-pressure Cases.—The treatment of low arterial tension which is secondary to long-existing high-tension conditions has two elements—first, the correction of circulatory errors by the action of drugs which have the power to modify physiological forces in various parts of the circulatory circuit, and, second, the restoration, as far as possible, of the health of the tissues upon derangement of which the trouble often rests.

In diseases of the circulatory apparatus attention is too often concentrated upon the first. In instances of temporary embarrassment, or of extra demands on account of complicating diseases, this first element becomes of supreme importance, but in the long run it is the second element upon which success in the care of circulatory disorders is dependent.

In this connection, it is important to differentiate between the symptoms and the disease. Dropsy of the dependent portions of the body is a symptom which does not always demand treatment. If of moderate degree, and dependent upon well-understood causes, it is often the part of good judgment to undertake the second element of treatment, neglecting for the time being the symptom, the removal of which would require intervention in the physiological activity of the heart, such as might neutralize treatment directed to the circulation as a whole; indeed, there is often much harm done in such cases by violent attacks upon symptoms.

Most writers on circulatory disease have passed over with scant consideration the management of cases with general edema and steadily progressive symptoms, which, if not checked, uniformly lead to a fatal termination. It is unscientific to disregard these cases in considering various forms of treatment at length, dismissing them with a single clause. This is frequently done in speaking of the Nauheim treatment, progressive cases being usually spoken of as unsuitable. There is always the possibility in any particular case that we may be mistaken in our estimate of it, and the patient is entitled to the treatment even at the risk of discrediting the system by the limitation of results because of the severity of the case.

In primary low arterial tension the heart muscle is in a position to recover its tone if depleted by acute

disease, or to develop a compensatory hypertrophy if overtaxed by defective valves. In secondary low arterial tension the heart has already for the time being exhausted its power of compensatory hypertrophy, and while the tendency to resistance in the arteries persists, there is no adequate response on the part of the heart.

Little is gained symptomatically in extreme cases by the use of vasodilators, because the blood-pressure is already low. Little is gained by digitalis, because the heart-muscle is not in a position to respond. The combination of drugs of the digitalis group with drugs of the nitrite group produces a certain amount of symptomatic response, but in the end does not produce permanent results unless combined with measures that will hold the advantage gained. Excessive drugging is a mistake. A single large dose of digitalis at night is often better than divided doses. A good fluid extract put into a capsule and swallowed at bedtime, the dose being determined by experiment, has often proved very satisfactory. Attention to the digestive organs is of the utmost importance. Milk is often badly borne and should be replaced with the most nutritious food that will agree with the patient.

As often as possible, these patients should be put upon a regimen directed to the improvement of nutrition and to the healthfulness of the body in general, such as hydrotherapy in the form of warm saline baths, a nutritious diet, planned to exclude a multiplicity of proteins, but not limiting the quantity of such as are known to be safe for the individual, and exercise in the open air up to the point where dyspnea interferes.

We are dealing often enough with dangerous conditions, and it is not possible to compare the result in a particular case with what it would have been under other circumstances. A man must be of limited experience indeed who has not seen such a patient do better when disregarding advice that planned treatment of such a condition by prolonged rest in bed, restricted diet, and excessive drug therapy.

Secondary low arterial tension is the final result of many causes acting along the line of those forces which tend to the termination of life in the natural course of events, hence it is to be combated, not by drugs alone, but by all those methods that are known to remove cachexia, and restore tone to the blood and solid tissues.

Louis Faugères Bishop.

Blood Root.—See *Sanguinaria*.

Blood Stains.—The identification of blood stains is a matter of interest chiefly in a medicolegal aspect. While the methods employed in legal tests are practically the same as those in use in general medical diagnosis, the elaborate precautions necessary to prevent errors make it impossible to use in the former some of the simplified procedures of the practitioner.

In criminal cases it is usually the custom for the officers of the police, the coroner, or the public prosecutor to search for and record the presence of blood stains in any condition in which their presence or identification may be of importance. While such a procedure is satisfactory in many cases, it is often of the utmost importance that the person who is to be called upon to make the final identification of the material should be permitted to investigate all suspicious stains before anything at the site of the accident or crime is disturbed. Much can be learned by an expert not only as to the conditions under which any blood may have been distributed over objects, but also as to the substances upon which such blood may have fallen, and thus the obtaining of specimens contaminated with material which may render further tests difficult or impossible will be avoided.

Under conditions which necessitate the further study of blood stains in order to determine whether the suspected material is human or animal blood, the stains, especially the finger prints, should be carefully photographed, the photograph including a millimetric scale and also a label written in black ink giving the exact site of the stain and the material upon which it has fallen. Such a record is more valuable than the most voluminous notes. Small articles on which blood has fallen should be inclosed either in clean writing-paper, the parcel being promptly labelled and sealed with sealing-wax, or, what is better, in glass bottles or clean paper boxes, these containers being sealed and labelled also. Newspaper is not a satisfactory material for this purpose. Under no circumstances should an inexperienced person be allowed to attempt the removal of blood stains from the underlying material, if biological or other tests are to be carried out upon the blood at a later time.

Stains on furniture, floors, steps, or boards of any sort should be removed by sawing out a considerable area about the suspected spots; the piece should then be wrapped in clean white paper, sealed, and marked as above. Stains on plaster should be chiseled out and sent as quickly as possible to an expert, as the lime in the plaster rapidly alters the blood so that biological tests cannot be applied. Cutting instruments should be fastened to a piece of board with the stains uppermost, and carefully wrapped. Clothing, especially if of a dark color, should have any suspicious stains marked by passing a pin near but not through the spot, and should then be wrapped and sealed. The reason for this marking is that blood spots which are at first of a fairly bright red may change in color owing to the action of light and air, or of the substratum upon which they lie, and in a short time become nearly invisible if on a brown or other dark surface.

In case the blood is spattered upon walls or objects so heavy that they cannot be moved, it may be necessary to scrape samples of the spots from the surface, using a perfectly clean knife blade and thoroughly cleaning the blade for each set of spots removed, in order to avoid the possibility of mixing two different specimens, and the specimens so removed should be preserved in clean glass-stoppered bottles or, less satisfactorily, in clean glazed paper.*

Fluid blood, as, for example, from a case of illuminating gas poisoning, should be collected and transported either in new clean preserve jars or in glass-stoppered bottles.

If fresh fluid blood is found soaked up by soil, sawdust, or other material, either a considerable amount of the contaminated substance is collected and placed in clean glass receptacles, or clean white filter paper is pressed against the mass so as to absorb some of the fluid and, after drying in the air, is inclosed in clean envelopes and properly labelled, care being taken to furnish exact details as to the material from which the blood was obtained, for such information may be of the greatest importance if biological tests are to be made.

Preliminary Examination of Suspected Material.—The specimens submitted for study should be most carefully scrutinized in order to obtain suitable material for examination and to avoid the commission of serious errors in the complicated tests now so largely employed in the identification of blood stains. Each suspected blood fleck should be scrutinized with a lens in order to see whether or not stains due to other substances are present. It is well known that saliva, perspiration, albuminous urine, menstrual fluid, feces,

* An example of the danger of allowing untrained persons to remove specimens for examination was shown in a case where some specimens gave precipitin reactions for both human and chicken blood. When the site was reexamined two sets of blood stains were found, one of which gave the reactions for human blood, the other a perfectly clear reaction for chicken blood. A mixture of the scrapings had evidently occurred.

pus, and similar body excreta may give a precipitin reaction, though much less intense than that of blood itself, and some of these fluids give recognizable stains. If, however, biological tests are to be employed in the identification of blood stains, the material for such tests should be if possible selected from areas where the likelihood of such contamination is the least. As such tests are at present conducted, only a fluid whose albumin content approximates that of the blood itself is likely to cause the slightest confusion, but it is better not to have to explain such facts in court, and much trouble can be avoided in medicolegal cases by care in the selection of the material for the test.

Rust marks on steel instruments are often difficult to distinguish from spots of blood, and occasionally brown or dark red paint may be confusing. In examining steel instruments it should be constantly held in mind that fresh blood can be easily and completely removed by washing, even though the process is hastily carried out. The writer has seen a club with numerous superficial cracks on the surface which was used to inflict a series of deep scalp wounds, and yet after a hasty rinsing in water no blood stains could be found upon the instrument.

If spots are found which seem suspicious a sheet of white glazed paper should be spread in a place free from draughts, and some of the suspected material scraped off with a clean sharp scalpel. Stains on cloth should be partially cut out with sharp scissors, leaving a portion for identification in court or as material for further tests should a repetition of any procedure be necessary. The samples so obtained should be preserved in small glass-stoppered bottles and kept in a dark cool place until examined.

Identification of Suspected Material as Blood.—Before carrying out any of the complex biological tests, the suspected material must be shown to be blood. There are a large series of reactions

Fig. 814.—Hemin Crystals Produced by the Acid-alcohol Method. × 300.

which are available for this purpose, but only those should be employed which are recognized by the standard authorities as reasonably free from error. It is especially important not to use the modern color reactions for blood, such as those with benzidin or phenolphthalein, for there are so many fallacies in the application of these reagents, that the reactions are utterly unsuitable for presentation in a court of law as fulfilling the requirements of legal proof.

One test which does fulfill all requirements is that of Teichmann, the only drawback being that it is often difficult to obtain this from blood which has long been in contact with iron, plaster, soaps, fats, or other organic material, especially if putrefaction has occurred. Therefore, while a positive Teichmann reaction occurs with no other substance than hemoglobin, a negative reaction does not prove the absence of blood.

Teichmann Test.—A very small fragment of the substance to be tested is scraped from the stain or if it has been deposited upon cloth a few fibers are teased free from the edge, and moistened with a drop of physiological salt solution on the surface of an ordinary microscopic slide. The preparation is allowed

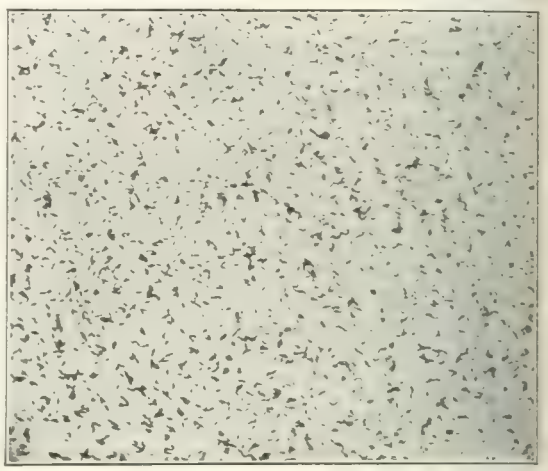

Fig. 815.—Hemin Crystals Produced by the Strzyzowski Method with Hydriodic Acid. × 300.

to dry spontaneously or the drying is aided by very gentle heat, and when it is perfectly desiccated it is covered with a drop of glacial acetic acid and a thin cover-glass. The preparation is then gently warmed until the acid is seen to assume a brownish color, after which the heating is continued at a lower temperature until the acid has evaporated. A little water is then run under the cover and the preparation is examined with a magnification of about 300 diameters. If the test is positive, small rhomboidal crystals of hemin will be seen, having a brownish color and angles of approximately 60° for the acute and 120° for the obtuse angle. The crystals frequently show rounded corners and even clubbed ends, however. If the quantity of blood is very small, regular crystals may not be obtained, but instead a crop of very small oat-shaped forms, often with curved outlines and no sharp angles, will be seen. This method is the original form of the test. If it fails there are two modifications which occasionally are more successful.

One of these is due to a suggestion of Wachholz, who recommends the employment of a mixture of equal parts of 95 per cent. alcohol and glacial acetic acid instead of pure glacial acetic acid. The addition of the alcohol reduces the boiling-point of the fluid and increases its solvent power for hematin, so that this pigment is more rapidly brought into solution. The final evaporation of the mixture is also carried out more easily owing to the volatility of the alcohol (Fig. 814).

The other modification is that of Strzyzowski in which a special reagent made up just before using is employed. The reagent is composed of glacial acetic acid, water, and ninety-five per cent. alcohol, 1 c.c. each, to which are added three to five drops of hydriodic acid of a specific gravity of 1.5. The substance to be tested is placed on a slide, allowed to dry, and then covered with a thin cover-glass. A few drops of the reagent are allowed to run under the

cover, and the preparation is warmed over a small flame for about ten seconds. The fluid is replaced as fast as it evaporates, and brought just to the boiling-point. The preparation is allowed to cool, and is then examined directly with a power of at least 300 diameters (Fig. 815). If no crystals are found, fresh solution is added, and the heating is repeated. This method is four times as sensitive as the original Teichmann test.

A somewhat similar method of identifying blood pigment, which may be useful when the Teichmann test or its modifications fail, is by the production of crystals of hemochromogen (Heine). The technique of the method is as follows: The suspected material, which should be reduced to a fine powder and separated as much as possible from fiber, especially wool dyed with indigo, rust, plaster, etc., is placed on a slide. A drop of a mixture of two parts of pyridin and three parts of a concentrated watery solution of hydrazin sulphate is added, and a cover-glass is laid on. The preparation is now very gently heated over a small flame until a few air bubbles appear, and then

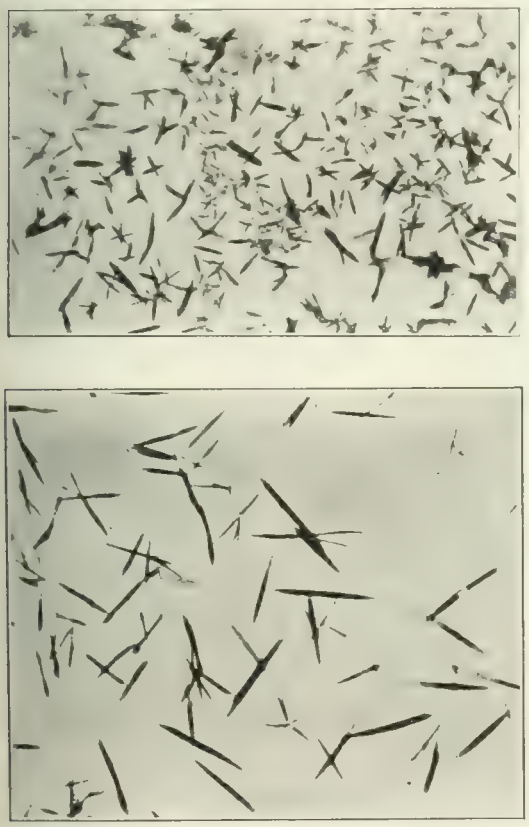

Fig. 816.—Hemochromogen Crystals. Two different types produced by varying rates of crystallization and concentration of blood. × 300.

is allowed to cool gradually on an asbestos plate or other non-conducting surface. The crystals which appear when blood is present in the preparation are in the form of fine needles or of fairly broad lancinate figures. They may be rectilinear or curved, and occasionally they show brush-like extremities. They may lie singly or in crossed forms or in sheaths or rosettes. The longest crystals are obtained with fresh blood. Occasionally some ovoid crystals resembling the hemp-seed type of hemin crystals may be noticed (Fig. 816).

If the blood is fluid it is not necessary to dry it. A drop of the reagent is added directly, the preparation is heated, and the crystals are observed. The preparation must be very carefully searched, and a high magnification may be required, even a $\frac{1}{12}$ oil immersion lens. An additional means of identification of the crystals lies in their optical properties. They are copper red in color, and when examined with a polarizing microscope show double refraction and pleochroism, with c = reddish brown, a = orange red, and c > a. The crystals also show straight extinction. By very carefully drying them and immediately adding a drop of Canada balsam, permanent preparations can be made.

The conditions which interfere with the production of hemochromogen crystals are in general those which affect the production of hemin crystals. If the blood pigment has soaked into the cloth or wood it is much more difficult to obtain the crystals than if a crust can be scraped off of the material. Sometimes, especially with old specimens which have undergone putrefaction, it is impossible to get satisfactory preparations. With fresh blood, on the contrary, excellent results can usually be obtained. Iron rust interferes less with the formation of hemochromogen crystals than with the formation of hemin crystals. A mixture of soap or fat does not interfere, and the crystals can be obtained from fecal or gastric matter. Carbon monoxide blood may or may not furnish crystals. When the blood is on fibers dyed with indigo, indigo crystals are occasionally obtained in doing the hemin test; this confusion does not arise with the hemochromogen method, which, therefore, should be adopted under these conditions.

Spectroscopic Tests for Blood.—An additional and most convenient method for the absolute identification of blood pigment is by the use of the spectroscope. For this purpose one of the smaller hand or "pocket" instruments is much more satisfactory than a spectroscope of high dispersive power such as is usually seen in chemical and physical laboratories. While the so-called "pocket" spectroscope is quite sufficient for the identification of blood spectra, a more convenient form is a "comparison" spectroscope, in which by a pair of prisms the light from two different specimens is sent through the same slit and the spectra are superimposed on each other. In one container is placed the solution to be tested, in the other a known dilution of blood.*

When very small quantities of blood are to be studied a microspectroscope may be useful. This instrument fits into the microscope tube in place of the ocular, and if a sufficiently high power objective is used is extraordinarily sensitive; the spectrum from even one blood corpuscle can be identified. A specimen of fresh blood or one which has dried for a short time, when dissolved in water, shows the two-banded spectrum of oxyhemoglobin, the maxima being at wave length 583 and 548 (see Fig. 817); but after the blood has dried for a longer time, especially if the stain has been on cloth, the pigment is changed into a substance known as methemoglobin, and an aqueous solution of the particle will give a spectrum combining methemoglobin and oxyhemoglobin or a pure spectrum of methemoglobin (see Fig. 817). This change is hastened by the action of sunlight, putrefaction, etc. During life methemoglobin may occur in the blood in cases of poisoning by potassium chlorate, phenacetin, acetanilide, nitrogen tetroxide fumes, etc., and these possibilities should be taken into consideration. Inasmuch, however, as both the oxyhemoglobin and the methemoglobin spectra are rather faint, it is an advantage in testing small quantities of material or when using very dilute solutions to convert the pigment immediately into a substance

* An exceedingly convenient form of "comparison" spectroscope is made by Hans Heele of Berlin, carrying two test-tubes for the solutions to be examined.

which gives a much greater absorption intensity. If it is transformed into hemochromogen, which is easily done by dissolving a particle of the suspected pigment in pyridin and reducing the solution so obtained with a drop of yellow ammonium sulphide, or what is preferable, with the same amount of a saturated solution of hydrazin sulphate, about one part of blood in 10,000 parts of water can be detected if a layer of solution one centimeter thick is examined.*

For the examination of these spectra with the microspectroscope the fluid is conveniently placed in a narrow cylinder made by cementing a piece of thick wall glass tubing, one or two centimeters in length, perpendicularly on an ordinary thick microscopic slide with Canada balsam, or temporarily with vaseline. If the lumen of the tube is narrow only a very small quantity of fluid is required to give the necessary depth for the absorption bands.

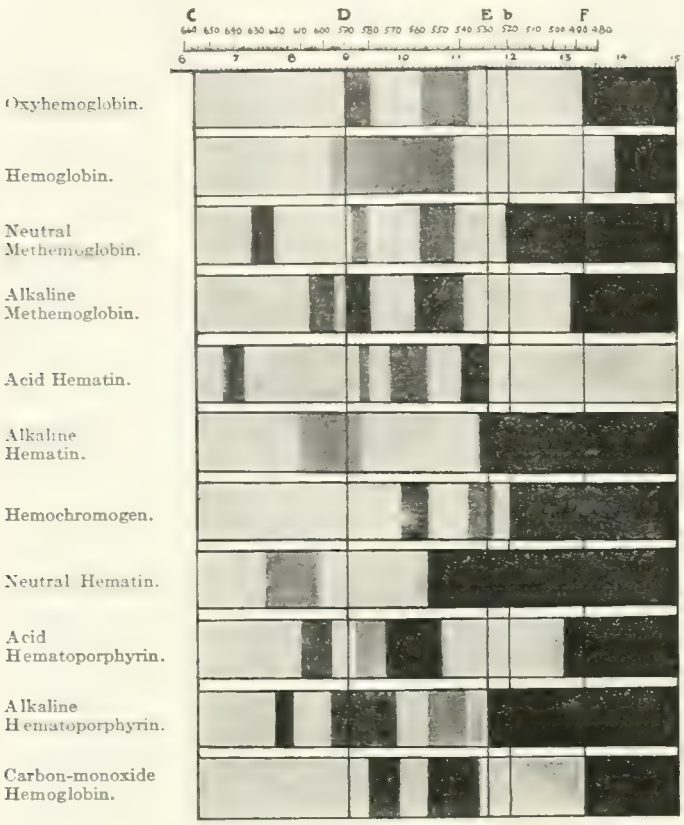

FIG. 817.—Absorption Spectra of Importance in the Identification of Blood.

If the blood is on cloth which has been boiled, washed with soap and water, or exposed to sunlight for a long time, the pigment may be altered into hematin which is insoluble in water and is best extracted by the use of ethyl ether to which one-third volume of glacial acetic acid has been added. Hematin is soluble in this fluid as acid hematin, the spectrum of which can often be recognized. If the ether is allowed to evaporate and a drop of the pyridin and hydrazin sulphate mixture mentioned above is added, the hematin will be changed into hemochromogen, the absorption of which is much more intense than that of hematin, so that the bands are much more easily seen. If the solution is deeply colored by extraneous matter it may be necessary to use intense light like sunlight to get sufficient illumination through the fluid. If turbid, the fluid must be filtered through a good quality of filter paper, such as Schleicher and Schüll No. 597, or, what is in many cases preferable, centrifugalized in a high-speed centrifuge until all sediment has been thrown to the bottom of the tube. The supernatant fluid is then pipetted off into a glass cell and examined.

If the blood has thoroughly soaked into a dyed cloth, it is sometimes extremely difficult to prevent solution of the dye at the same time that the blood is dissolved, and this is especially true in the case of old blood spots where the longer the maceration necessary to dissolve the blood, the more pigment goes into solution from the cloth. It is often quite impossible by extraction with pyridin or a strong alcoholic solution of potassium hydrate to get a satisfactory hemochromogen spectrum. In this dilemma a solution of the cloth and stain together can be obtained by maceration of the cloth fragments in concentrated sulphuric acid, and then by filtering the fluid through glass wool and diluting the filtrate with ten to twenty volumes of distilled water; the hematoporphyrin formed by the action of the acid is precipitated, whereas the dye from the cloth remains in solution. After the hematoporphyrin has settled, it is washed with several changes of water, collected, and dissolved in warm strong sulphuric acid, the solution giving the absorption of acid hematoporphyrin. If the precipitate is dissolved in a mixture of equal volumes of ten-per-cent. sodium hydrate and alcohol, or in pyridin, the solution will give the absorption of alkaline hematoporphyrin.

Full directions which will meet all conditions cannot be given here. It must be left to the ingenuity of the expert to devise means to fit special cases. Usually from the specimens submitted, samples of the cloth can be obtained sufficient to allow a series of experiments as to the effect of the various extracting fluids upon the dye; and then small blood spots can be made on the cloth and attempts made to recover the blood pigment. After a satisfactory method has been devised it can be applied to the suspected deposits.

Examining Stains for Cellular Constituents of Blood.—While in the past a large amount of medico-legal interest has centered about the identification of blood corpuscles in blood stains and the careful measurement of such corpuscles when properly mounted, at the present time but little value is placed upon the results so obtained. Leucocytes can be demonstrated by fixing a small piece of the clot with alcohol or formalin, staining with hematoxylin, clearing, and mounting, just as in the methods employed in pathological histology, but this procedure does not give us facts of any great value. Of softening solutions for blood stains which to a certain extent permit the separation of the red corpuscles and their identification microscopically, the most important are a thirty-three-per-cent. aqueous solution of potassium hydrate or a mixture of pepsin and strong glycerin, which can be purchased from Grübler. In general, the thirty-three-per-cent. caustic potash is perfectly satisfactory. A little of the stain or of the cloth on which it lies is softened, scraped off, and placed under a microscope, and the corpuscles examined. Inas-

* If a microspectroscope is not available, the absorption bands can frequently be demonstrated by the use of an ordinary hand spectroscope looking down through the microscope either with or without the ocular.

much as the red corpuscles of the horse, dog, pig, guinea-pig, rabbit, and mouse have practically the same dimensions as human red corpuscles, and those of cattle are but little smaller, it is evident that even careful measurement of the corpuscles is of little value, especially when the shrinkage due to drying and the swelling following re-solution of the blood are taken into consideration. It is possible, however, to recognize the oval and nucleated red corpuscles of avian and reptilian blood.

Florence has suggested a method for identifying corpuscles without recourse to the softening process, using a so-called vertical or opaque illuminator, by which a strong beam of light is reflected downward through the objective by a suitable prism, and opaque objects thus rendered visible. It is possible with suitable material to obtain quite satisfactory photomicrographs up to a magnification of 1300 diameters. The chief advantage of this procedure is that the blood stain is not destroyed, and it is always possible to use the whole specimen for further tests.

All of these methods, however, are medicolegally of no importance compared to the highly sensitive procedures lately discovered, of which the best example is the precipitin reaction. This will form the subject of the next section.

Precipitin Reaction for Identification of Blood Stains.—It was found by Bordet and Tchistovitch about 1897 that certain animals when injected with blood from other animals developed, after a certain definite period, the power of precipitating the blood serum of the animal from which the blood for injection was originally obtained. For example, if human blood is repeatedly injected into a rabbit, the blood serum of the rabbit finally develops the power of forming a cloud in human blood serum in very high dilutions, even 1 to 20,000. This reaction is quite specific, antihuman serum giving a strong precipitate with human blood, only a faint precipitate with the blood of the higher apes, and practically none at all in dilutions of 1 to 1,000 with the blood of the smaller monkeys. Similar group reactions have been noted among other animals (Nuttall); for example, an antiserum prepared by injecting chicken's blood will give a very faint precipitate with the blood of other birds, but not in such a degree as to interfere completely with the medicolegal value of the test.

Preparation of the Antiserum.—The rabbit is the animal generally employed for the production of antiserum, and large, healthy, long-eared ones should be selected for the purpose. Young animals usually react better than old ones. They should be well fed and kept in a clean dry place.

Fresh sterile human blood is injected in quantities of 2 to 6 c.c. into the ear vein of the animal. If tests to determine whether the blood is from any of the domestic animals are also to be made, specimens of their blood may be obtained from slaughter houses or elsewhere. If blood from adult human beings cannot be obtained it is possible to use that from the placenta. By placing the placental end of the cord in a sterile cylinder and causing the uterus to contract by pressure, a number of cubic centimeters of sterile blood can be obtained. Blood may also be obtained at fresh autopsies by opening the heart. Even dry blood has occasionally been used with success, but the most satisfactory method is the use of perfectly fresh blood drawn from a vein into a sterile syringe and immediately injected into the animal. The amount required is not very great and such blood is usually obtained easily from suitable subjects. If there are any doubts as to the sterility of the blood it is an advantage to heat it in a water bath at 56° C. for an hour.

As stated above the intravenous method of injection is preferable, though the blood may be injected subcutaneously or intraperitoneally. Usually, however, the quality of the antiserum in the latter cases is inferior to that obtained by intravenous injection. The technique of injection is simple. The ear of the animal is shaved, washed with soap and hot water, and rubbed with alcohol. This will, as a rule, cause considerable distention of the veins of the outer surface of the ear, and if the ear is then firmly supported over the side of the left index-finger, the needle of the syringe can be easily inserted. The blood should be warm and should be injected slowly. The animals seem to suffer no discomfort from the injection.

The number of injections required to produce an antiserum of high titer varies with different animals. In some it is absolutely impossible to obtain a satisfactory serum, and they have to be discarded; while other animals quickly give a serum of 1 to 4,000 titer. Different workers have slightly different methods of immunization. Some prefer considerable quantities given on three successive days, the animal being bled on the tenth or twelfth day. Others give small doses, increasing them slowly, and administering them every third day, bleeding taking place at the end of two weeks. Before the final bleeding is done, however, the serum should be carefully tested with known dilutions of the blood against which the antiserum is specific.

Leers thinks that the best results are obtained by injecting 2 c.c. of blood intravenously, repeating the injection at the end of three weeks, ten days later drawing about 10 c.c. of blood and testing the titer, and then reinjecting another 2 c.c. of the same blood. In this way he usually gets an antiserum with a titer of 1 to 20,000. He thinks it is an advantage to use for the injections the blood from the same person and not from different people.

Obtaining Samples of Blood for Testing.—The animals should be starved for twenty-four hours, so that the serum will be perfectly free from fat and clear. The ear is cleansed, the veins are dilated by rubbing with ether, xylol, or alcohol, and a few cubic centimeters of blood are drawn off in a small syringe by puncturing the vein, or by making a V-shaped cut with a pair of scissors and allowing the blood to run into a sterile test-tube. The flow is freer if the animal is kept warm on a hot water bag and the head is lowered; or the ear may be warmed by holding it against a lighted electric bulb. The blood is caught in small sterile tubes, which are immediately laid in a slanting position until the blood coagulates and then set vertically in a cool place for twenty-four hours. The separation of the serum does not take place as satisfactorily in the ice box as at room temperature.

Testing the Titer of the Antiserum.—Fresh blood of the species for which it is desired to test is obtained and diluted with distilled water in the proportion of 1 to 500, 1 to 5,000, and 1 to 10,000. To these dilutions are added equal volumes of 1.7 per cent. sodium chloride solution so as to bring the final salt content up to 0.85 per cent. Nine-tenths cubic centimeter of each of these dilutions is put into small perfectly clean test-tubes with a lumen of about six millimeters, and 0.1 c.c. of the antiserum to be tested is allowed to run down the side of the tube. If the serum is satisfactory it will usually give a precipitate in the 1 to 10,000 dilution within a couple of minutes, the cloud beginning first at the point of contact between the diluted fluid and the drop of serum which has fallen to the bottom of the tube, and quickly spreading up through the fluid as the specific serum diffuses into the diluted blood. A serum giving a precipitation in a dilution of 1 to 20,000 is very rarely obtained. If the titer is below 1 to 1,000, the serum is unsatisfactory and the animal should receive a few more injections and then be again tested. If a titer of 1 to 1,000 is not then obtained, the animal must be rejected, and fresh ones immunized.

Obtaining the Antiserum.—After the blood of the animal is found to give a precipitate in sufficiently

high dilutions, the serum may be collected. For this purpose the animal is anesthetized, the neck is shaved and sterilized, and either a glass cannula with a rubber tube is inserted into the carotid, or the needle of a large glass syringe is plunged into that vessel, care being taken to have loose ligatures about the vessel so as to check hemorrhage in case the needle or cannula slips. From 50 to 60 c.c. of blood may be drawn into a series of Petri dishes, Erlenmeyer flasks, or test-tubes, the last being promptly slanted so as to give as large a surface for exudation of the serum as possible. The best yield of serum seems to be from the large Petri dishes. The blood is then placed in a cool spot, and as soon as the serum collects it is removed in a sterile pipette to final receptacles for storage. These may be either small test-tubes of brown glass measuring 12.5 centimeters in length by 7 millimeters in diameter, as recommended by Uhlenhuth, or glass bulbs with long narrow tubes on either side through which the blood is sucked up into the bulb, both of the tubes then being sealed off. All of the glassware must be thoroughly sterilized. The serum is kept on ice in the dark, but even with these precautions gradually loses its precipitating power.

It is extremely difficult to sterilize this antiserum without altering it in any way, and the utmost care should be taken in all procedures to keep the fluid absolutely free from organisms. If it is necessary to sterilize it, this must be done by filtration through a Berkefeld filter, using the smallest size filter and regulating the suction so that not more than one drop carries through every five seconds. Otherwise, bacteria are sucked through the pores of the filter.

Many suggestions have been made for the preservation by desiccating the serum in a vacuum or by drying it on filter paper, but without great success. The blood of the animal does not retain its high precipitating power for any great length of time, so that it is impossible to keep the serum so to speak *in vivo*. A gradual fall takes place and finally the precipitating qualities disappear. The animals, however, can be immunized by a fresh series of injections, and therefore should not be destroyed.

The separated antiserum, which may amount to 10, 20, or even 30 c.c. from a single large rabbit, is finally most carefully controlled by dilutions of blood made by measuring off a given volume of fresh animal or human blood, and laking it in a known volume of distilled water. For this purpose the mixing pipettes of the Fleischl-Miescher hemoglobinometers are useful. After laking, exactly double the amount of 0.85 per cent. sodium chloride solution is added, so as to bring the salt content of the fluid up to the norm of 0.85 per cent. A series of tubes are then set up containing 0.9 c.c. of blood of known dilutions from 1 to 1,000 to 1 to 30,000, and 0.1 c.c. of the perfectly clear rabbit serum is added. In order to be considered satisfactory the reaction must occur in these tubes within five minutes. The serum may be used if the reaction occurs in the 1 to 1,000 dilution only, but it is better if possible to obtain a higher value. One-tenth cubic centimeter of the antiserum is mixed in a tube with 0.9 c.c. of clear sterile salt solution as a control, and in other tubes tests of the antiserum are made against dilutions of dried blood, against the serum of the inoculated animal, in this case the rabbit, and also against extracts in physiological salt solution of the substances upon which or in which the blood is found. If, for example, the blood is on cloth, an extract of this cloth free from any stain should be made. When the antiserum is found to give a cloud only with the specific blood against which it is to be tested, suitable solutions are made from the blood clot and tested by the method just outlined.

Final Tests and Controls.—The stain is cut out of the cloth or other substance on which it lies, and tested by the spectroscope or by the formation of crystals for blood. A portion is then dissolved in 0.85 per cent. sodium chloride solution. If no apparent solution takes place, distilled water may be used, but it may take hours to effect solution in either of these substances. In case the process is slow, the whole may be transferred to the ice box and left over night. The solution so obtained is tested with litmus paper and rendered exactly neutral with sodium carbonate or tartaric acid as may be necessary. Finally, it is filtered through a small Schleicher and Schüll filter No. 597. In case of persistent opalescence it may be necessary to centrifugalize the solution in a high-speed centrifuge. The concentration should be as nearly as possible 1 to 1,000. The best way to judge of this is to shake a small quantity of the solution in a test-tube, when, if it is of about this concentration, it will foam; it will also give a very slight cloud on the addition of one drop of twenty-five per cent. solution of nitric acid. If the blood is more concentrated than this the formation of a precipitate may be inhibited. The reaction is carried out in small test tubes measuring about ten centimeters long and eight or nine millimeters in diameter. These tubes must be absolutely sterile and clean. The best method of cleansing is to soak the tubes for some time in a mixture of one volume of concentrated hydrochloric acid and four volumes of ninety-five per cent. alcohol. The tubes are then rinsed in distilled water to remove the acid, drained, and sterilized in a glass container by dry heat at 150° C.

A series of such tubes is then set up in a rack, numbered with a wax pencil, and filled as follows:

1. 0.9 c.c. of a 1 to 1,000 solution of the blood to be tested.
2. The same.
3. 0.9 c.c. of a 1 to 1,000 solution of fresh normal human blood in 0.85 per cent. sodium chloride solution.
4. 0.9 c.c. of a 1 to 1,000 solution of dried human blood in 0.85 per cent. sodium chloride solution.
5. 0.9 c.c. of a 1 to 1,000 solution of horse blood in 0.85 per cent. sodium chloride solution.
6. The same of chicken blood.
7. The same of dog blood.
8. The same of cat blood, and so on, using the blood of any animal which may be suspected as the source of the stain.
9. 0.9 c.c. of sterile 0.85 per cent. sodium chloride solution.
10. 0.9 c.c. of an extract of the cloth, paper, wood, or other substance upon which the stain was found.

To each of these tubes, with the exception of 2, 0.1 c.c. of the antiserum is added with an accurately graded pipette. To tube 2 is added 0.1 c.c. of clear normal rabbit serum.

In about two minutes a delicate cloud will appear at the bottom of the tubes containing human blood, with the exception of 2. In all others no cloud will appear. The tubes should be placed in a rack so that they can be conveniently held against a dark background, preferably black velvet. Under these conditions the faintest cloud will be visible.

Sources of Error.—In some cases it is difficult or impossible to obtain a satisfactory biological reaction. If the blood has been exposed to sunlight for any time, the reaction may, for some unknown reason, completely fail. If the blood has been dried on leather the results are less reliable because the tannin may produce spontaneous precipitates without the addition of the antiserum. Stains removed from wall paper are unsatisfactory. The starch used in laundry work may interfere considerably with the test. Mortar, fresh plaster, and lime destroy the precipitable substance of the blood. Acids and alkalies also interfere considerably with the test.

As can easily be imagined, with so sensitive a test as the one described above, many difficulties and much confusion may arise if the procedure is not carried out with the utmost care. In the first place,

it should not be forgotten that an antiserum produced by the use of blood as an antigen will react not only with blood, but also with milk, spermatic, menstrual, and lochial fluids, pus, sputum, and muscle protein, in fact with all the proteins of the organs and the secretions and excretions of the body. The greatest care must be taken, therefore, to see that the blood or substance tested is free from foreign mixtures. It must be ascertained also by inquiry as to the circumstances of the case whether it is possible that the substance which is suspected of being human blood may be mixed with or may be entirely composed of the blood of one of the higher apes. This, of course, can occur only under most unusual circumstances, in the neighborhood of a circus or of zoological gardens, for example, but it must be taken into consideration from a strictly legal aspect. If the possibility exists, then a specific serum must be made by injecting a rabbit with blood from one of the species of ape suspected. It has been suggested that by mixing an antiserum specific for human blood with the blood of an ape, and filtering off the precipitate so produced, a fluid will be obtained which is specific for human blood only. This somewhat complicated procedure, however, has not proved useful.

It has been shown that mixtures of other blood do not interfere with the specific reaction; that is, human antiserum will produce a precipitate in a mixture of dog and human blood.

It is not always possible to state that a specimen of blood which has been tested is from a particular one of a closely related group. For example, it is very difficult to distinguish between sheep, goat, and ox blood, between chicken, duck, and turkey blood, between rabbit and hare blood, between dog and fox blood, owing to the relatively close biological relationship between the members of these different groups. If special antisera are prepared from the blood of each species, such separation is often possible, but only with considerable difficulty; and in medicolegal work it is not as a rule required, the point to be determined being merely whether the specimen is or is not human blood. Of course, bird or fish blood is easily distinguished by morphological examination showing the presence of nucleated corpuscles, and such examination may in some cases save making up antisera for these special bloods.

In reporting the results of tests it is wise to state that a given blood is either that of a human being or of one of the higher apes. This may save explanations on cross examination. While contamination with the blood of the small monkeys must often be thought of, yet such blood rarely gives a reaction even in a dilution of 1 to 1,000, its biological relationship with human blood being much less close than that of the higher apes.

Detection of Blood by Complement Fixation.—A further biological method has been suggested for the identification of blood based upon the fixation of complement by the specific antigen under certain conditions. This method, while it has been successfully applied by Wassermann to the diagnosis of syphilis, is extremely complicated, and the liability to error is greater than with the precipitin test, so that in its present development the method cannot be considered as sufficiently reliable for medicolegal tests.

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Blood-vascular System, Origin of.—The whole circulatory system of the vertebrates—the heart, blood-vessels, and lymphatics—is lined by a layer of thin, flattened cells, known as the vascular endothelium. This endothelium constitutes the whole wall of the capillaries, but in the larger vessels and the heart it is covered externally by various layers of muscle fibers and connective tissue.

The development of all parts of the system begins with the formation of the endothelium and the other layers are added afterward. The present article deals with the origin of the endothelium only. The endothelium and the blood corpuscles have a common origin in certain *blood cells* which, in the vertebrates that have been studied at a sufficiently early stage, appear to arise for the most part in that region of the embryo or the blastoderm where the ventral mesoderm lies upon the yolk-laden cells of the endoderm. These primitive blood cells form collectively the rudiments of the whole circulatory system—that is, the endothelial channels and their cellular contents. To this fundamental tissue His (1900) has given the name *Angioblast*.

At its earliest recognizable stage, the angioblast is composed of solid masses of cells that lie in the cleft between the endoderm and mesoderm. Some preparations seem to show conclusively that these cells are of endodermal origin, while equally good specimens of other species, or even other parts of the same individual, demonstrate with equal clearness that the blood cells are differentiated from the mesoderm. It is, therefore, still an open question whether the angioblast is of endodermal, mesodermal, or of mixed origin.

In the holoblastic Ichthiopsida (amphibia, cyclostomes, and Dipnoi) the first appearance of the angioblast is a broad band of cells extending under the ventral mesoderm along the midline of the embryo from the anus to the rudiment of the liver. This band is bifurcated at both ends. The anterior branches extend forward on each side of the rudiment of the liver and unite with the paired rudiment of the heart.

The endothelium of the heart, according to Mollier (1906), is derived from paired rudiments, each consisting of a chain of cells appearing between the endoderm of the pharynx and the splanchnic mesoderm. These rudiments unite in the middle line between the oral pouch and the liver diverticulum (Fig. 818). The united portion which, at first, is wider than long, is the rudiment of the endothelium of the heart. From this, two strands of cells extend forward, one on each side of the mouth region. These are the rudiments of the mandibular arteries, or first aortic arches. In like manner, two strands of cells extend backward around the hepatic diverticulum. They are the rudiments of the omphalomesenteric veins, and connect with the anterior bifurcation of the ventral band of the angioblast.

The development of the tubular heart presents three stages: (1) The solid stage when the rudiment consists of a mass of loosely connected cells of irregular form; (2) the mesenchymatose stage, when the cells become separated, forming a syncytial network with protoplasmic bridges and irregular spaces between; (3) tubular stage when the cells have arranged themselves in a single layer surrounding the lumen of the heart.

In the triton embryo, according to Mollier (1906), at the time when the heart is in its earliest stages, isolated angioblast cells appear between endoderm and mesoderm at various places along the sides of the embryo, but especially near the boundary between the lateral and the ventral mesoderm.

The ventral band of angioblast is the so-called "blood island." The cells in the peripheral portion of this band develop into an endothelial tube, the subintestinal vein, while the cells that are enclosed

in this vessel become blood corpuscles. This is the sole source of blood in the young embryo. All the rest of the angioblast gives rise to empty vessels which, by anastomosis, become connected with the subintestinal vein and receive their blood from it. According to Mollier the angioblast cells that form the aorta and cardinal veins arise *in situ* on the inner

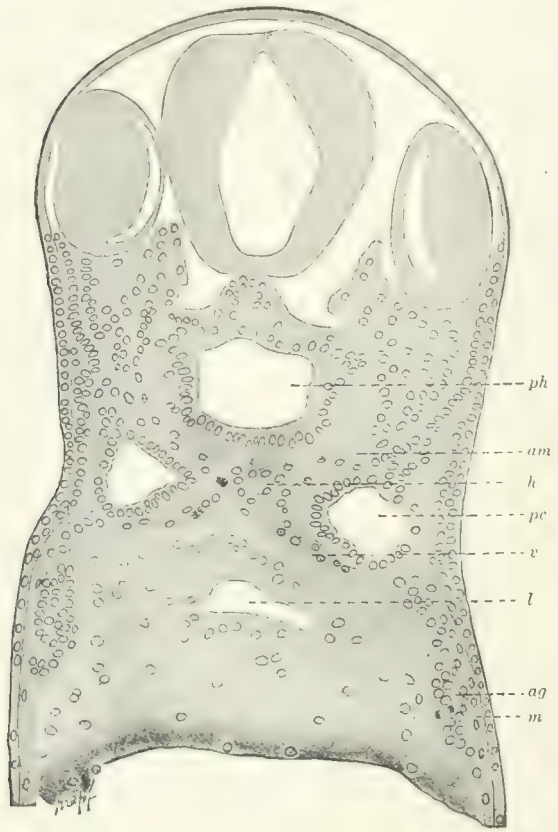

Fig. 818.—Frontal Section of a Triton Embryo with Nineteen Segments. *ag*, Anterior branch of ventral band of angioblast; *am*, mandibular artery; *h*, heart; *l*, liver; *m*, mesoderm; *pc*, pericardium; *ph*, pharynx; *v*, omphalomesenteric vein. (After Mollier.)

surface of the mesoderm, and have not wandered in from the ventral side.

In the amphibia and other vertebrates that have holoblastic eggs, the whole ovum develops into the embryo, and in these the development of the blood-vascular system is of the primitive type that has just been described. In contrast with this, we have the type found in the animals with meroblastic eggs (see Segmentation of the Ovum), including the majority of the fishes, the reptiles, and the birds, and also the mammals which, although having usually holoblastic eggs, follow the Sauropsidian type of development. In these animals, the blastoderm (*q.v.*) is divided into two portions, the embryonic and the extraembryonic. The latter portion forms the wall of the yolk-sac and it is here that the angioblast makes its first appearance.

In all of these vertebrates, as in the amphibia, the angioblast cells are differentiated in the cleft between the inner layer of the mesoderm and the endoderm. Moreover, this takes place under that part of the mesoderm that represents the ventral mesoderm of the amphibia, namely, the portion surrounding the posterior end of the primitive streak.

The chick may be taken to represent the type of development of the higher animals. At a very early stage, when the blastoderm shows little more than the primitive streak, the beginning of the angioblast formation is visible at the semicircular edge of the mesoderm as it grows backward over the area opaca. The angioblast makes its appearance as a collection of irregular plates of cells or, rather, a network with thickened nodes (Fig. 819). In section, these angioblast plates are seen to be two or three cells thick, and to be composed of cells that are more compact and rounded than those of the undifferentiated mesoderm. In later stages, the network extends forward along the sides of the blastoderm. The plates, or nodes, become thicker and are known as *blood islands*. The blood islands are confined to the area opaca, or very nearly so. They are connected by small strands of cells, *angioblast cords* (Bremer, 1912), which also invade the area pellucida and extend into the embryo. The connection of the extraembryonic angioblast with the body of the embryo begins at the anterior end, where the angioblast network of the area pellucida is connected soon with the rudiments of the heart.

The heart of all vertebrates begins as a pair of rudiments which pass through the three stages previously described and eventually unite in the midline under the pharynx. This union occurs during the solid stage in Ichthiopsida, during the mesenchy-

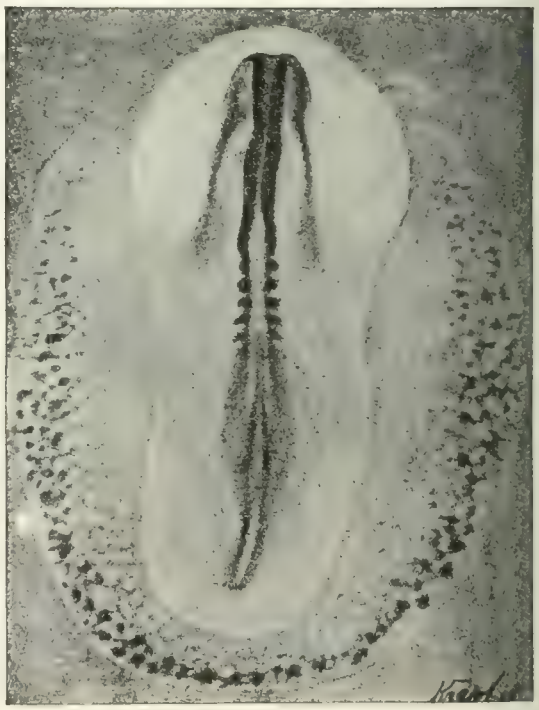

Fig. 819.—Blastoderm of a Chick with Six segments. Blood islands are visible as irregular dark spots forming a semicircle about the posterior end of the embryo near the edge of the area vasculosa. × 20. (After Ruckert.)

matose stage in the Sauropsida, and in the tubular stage in Mammalia.

When the chick embryo has reached the stage of seven somites, the blood islands begin to acquire a lumen. Beginning on the side of the island next the yolk, the superficial cells become flattened and form an endothelium which soon becomes separated from

the central mass of cells. The latter produce hemoglobin, and, after undergoing certain structural changes, separate as blood-corpuscles. The blood islands are the sole source of blood during the early part of embryonic life. At the same time, the angioblast cords are changing into endothelial tubes and this process is continued through the cords of the area pellucida to the embryo, until the greater part of the

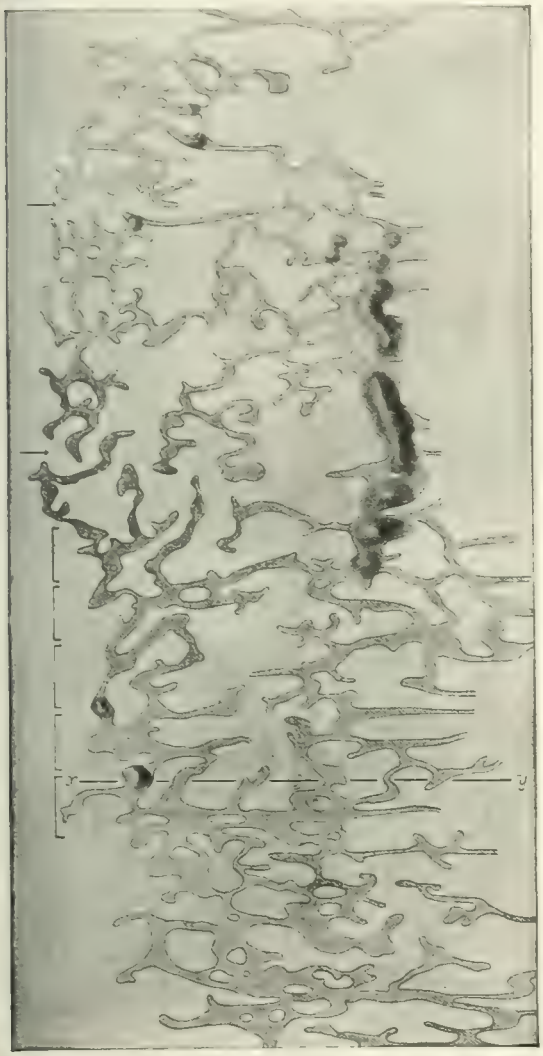

Fig. 820.—Reconstruction of the Angioblast from Sections of the Anterior Two-thirds of the Body of a Rabbit Embryo with Five Segments (8¼ days). The angioblast is represented as seen from the endodermal cavity with the median line of the body to the left and the solid cords growing in from the yolk sac to the right. Hollow vessels are indicated by shading. The largest of these is one of the rudiments of the heart. Brackets show the position of the somites and arrows indicate where the aortic net work is not yet complete. × 118. (After Bremer.)

angioblast is converted into a system of capillary blood-vessels, including the blood islands and the heart, and the circulation is established. The change from angioblast cords to hollow vessels is not, however, always a continuous process (Rückert, 1906, p. 1107). On the contrary, hollow spaces, *angiocysts* (Bremer, 1912), appear here and there in the network and afterward become confluent

Concerning the origin of the blood-vessels in the body of the embryo of the higher vertebrates, there are three principal theories; (1) The theory of His (1900) that they are formed by ingrowth of angioblast cords from the extraembryonic plexus; (2) the theory of Rabl that the entire vascular system is derived from outgrowth from the rudiment of the heart; and (3) the theory of P. Mayer and Rückert and Mollier (1906) that the heart and principle vessels are differentiated *in situ*.

Each theory has its adherents, but the first has received important confirmation by Bremer (1912), who has shown conclusively, by the method of reconstruction, that, in the rabbit at least, the whole vascular system of the body including the endocardium is derived from angioblast cords that grow in from the extraembryonic plexus (Fig. 820). The paired rudiments of the heart, "lateral hearts," appear as angiocysts in the network of angioblast cords before the pharynx is folded off from the general endodermal cavity and are subsequently brought together in the middle line by development of the head fold.

Little is known concerning the early stages of the blood vascular system of man. Spee's embryo von Herff (see Allantois, Fig. 76) has well-developed blood islands scattered over the entire ventral surface of the yolk-sac, and in the connective stalk and chorion there is a network of cells suggesting angioblast cords. Some doubt, however, as to the identification of the latter is caused by the fact that similar cells are found in the chorion of a younger embryo described by Fetzer, in which there is no indication of blood islands. If these cells in the Fetzer embryo are angioblast, we have in man a remarkable departure from the usual order of development of the blood-vessels. Spee's embryo, Gle (see Allantois, Fig. 78), has not only blood islands on the yolk-sac and angioblast in the connective stalk, but also typical paired rudiments of the heart and indications of angioblast cords representing umbilical arteries. The Eternod embryo, 1.3 millimeters long, has a heart, two dorsal aortæ, and a pair of umbilical veins. Apparently at this early stage of the human embryo the circulation is already established.

That the lymphatic system is a part of the general vascular system, and not derived from tissue spaces, was demonstrated by Sabin (1902) when she discovered that the lymphatics have their origin in outgrowths from the veins. It was subsequently shown (Lewis, 1906), that these outgrowths are at first capillary plexuses, and therefore, the whole lymphatic system is to be regarded as a derivative of the angioblast. Robert Payne Bigelow.

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Blood-vessels, Histology of.—The blood-vessels form a continuous branching system of tubes, which convey the blood from the heart by means of the arteries and capillaries to all parts of the body, then back again by the veins to the heart.

More recently the name of precapillaries has been used by some authors to designate the small vessels which pass from the arteries to the capillaries and from the capillaries to the veins and which were formerly known as arterioles and venules.

The Arteries.—An artery consists of three coats which, named from their relative position, are the inner, the middle, and the outer. The structure and

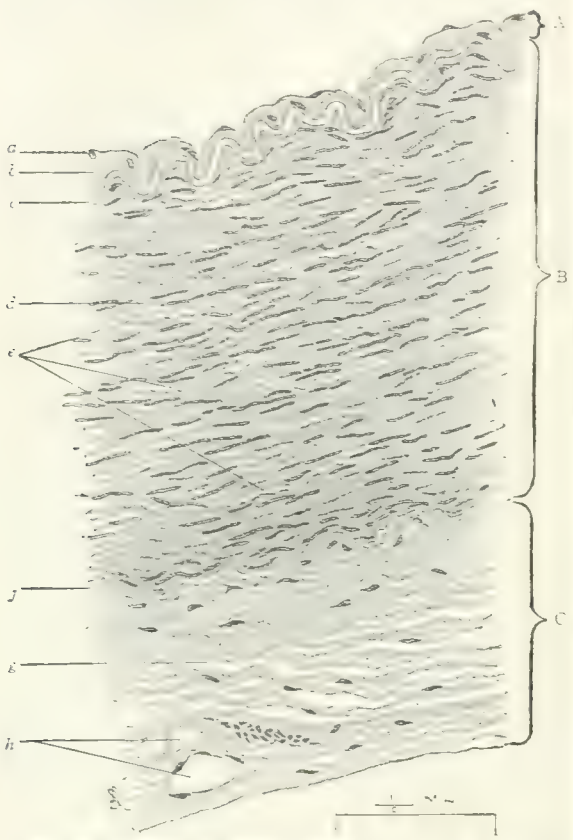

Fig. 821.—Section of Human Radial Artery. A, Intima; B, media; C, adventitia; *a*, endothelium; *b*, subendothelial tissue; *c*, internal elastic membrane; *d*, involuntary muscle; *e*, elastic tissue; *f*, external elastic membrane; *g*, fibroelastic tissue; *h*, vasa vasorum.

relative thickness of these coats vary in vessels of large, medium, and small caliber. A medium-sized artery, such as the radial, shown in the accompanying illustration (Fig. 821), has been taken as the type and first described in detail, the structural peculiarities of the larger and smaller vessels being subsequently noticed.

The *inner coat*, or *tunica intima*, is the thinnest coat of the artery and consists of three distinct structures: (*a*) an endothelial lining; (*b*) a layer of subendothelial connective tissue, and (*c*) an internal elastic membrane.

(*a*) The endothelial lining consists of a single layer of flat endothelial cells, each containing a centrally situated nucleus of round or oval form. When examined in a transverse section of the vessel, in which the cells are seen in profile, the endothelial plates are inconspicuous, the nucleus often being the only part of the cell readily made out. Examined from the surface, after staining with silver nitrate, the boundaries of the individual cells are clearly defined by the darkly tinted cement substance which unites the endothelial plates. In such preparations the lining cells appear spindle-shaped or lanceolate in form, their long axes corresponding with that of the blood-vessel. Careful examination of the outlines of the cell shows these to be serrated or sinuous, contrasting with the more regular lines of apposition in epithelial tissue. The lining cells of blood-vessels were first described by Kölliker and others as epithelium; later, His applied to them the name endothelium as more appropriate for elements derived from mesoderm and closely related to serous surfaces. In principle, endothelial cells are modified connective-tissue elements.

(*b*) The subendothelial layer consists of bundles of white fibrous connective tissue interwoven with a delicate network of elastic fibers, and meagerly distributed branched connective-tissue corpuscles lying within the lymph spaces of the tissue.

(*c*) The internal elastic membrane appears in arteries of medium size as a structureless, glistening, corrugated band that stands out as the most conspicuous structure of the intima. It constitutes the most external layer of the latter and forms a sharp line of demarcation between the narrow and faintly stained intima and the broad and more deeply tinted media. While apparently a homogeneous membrane in the smaller arteries, in vessels of large size the internal elastic membrane is represented by a number of delicate lamellæ of elastic tissue, which are pierced by apertures of varying size. The entire structure in these cases has been appropriately named the *fenestrated membrane of Henle*, in recognition of the anatomist who called attention to its peculiar arrangement. The majority of the elastic fibers forming this reticulated network run longitudinally, but are intermingled with some oblique fibers as well as a limited number of branched connective-tissue corpuscles.

The *middle coat*, or *tunica media*, is the thickest coat of the artery. It consists of circularly disposed lamellæ of involuntary muscle (*d*) intermingled with connective tissue in which elastic fibers (*e*) are conspicuous. The individual muscle cells are irregularly spindle-shaped, often with ragged outlines, and possess the characteristic rod-shaped nuclei. The muscle cells of the media are shorter and thicker than the slender and more elongated corresponding elements in other localities. The individual cells, held together by interstitial cement substance, are grouped into illy defined bundles, which are closely associated with small spiral bundles of white fibrous and elastic connective tissue, the whole forming the most compact coat of the artery. The elastic fibers are very numerous, and, in ordinary preparations being almost unstained, stand out in marked contrast among the more deeply stained masses of involuntary muscle.

The *external coat*, or *tunica adventitia*, is composed of closely felted bundles of white fibrous and elastic tissue (*g*) arranged in fine wavy masses. Many of these bundles have a longitudinal direction, while others pursue an oblique course. Connective-tissue cells are present in considerable quantity. While looser in texture and apparently of less strength, the adventitia is nevertheless more resistant than either of the other coats, and is the tunic upon which the integrity of a ligature chiefly depends. The walls of the arteries are nourished by a special system of minute vessels, the *vasa vasorum* (*h*), which enter the adventitia and penetrate the media. The vasa vasorum do not spring from the vessels which they supply, but are usually derived from neighboring arteries, the blood flowing through the larger vessels having as a rule no direct relation with that within the vasa vasorum.

The differences distinguishing the coats of a large artery from those of a vessel of medium size consist, in general, of an increase in the thickness of the various tunics, as shown in the accompanying Fig. 822.

The immediate lining of even the largest arteries consists of a single layer of endothelial cells; the subendothelial tissue, however, is greatly thickened not only relatively but also absolutely. The subendothelial bundles of white fibrous tissue are coarser, and the elastic tissue is present in greater amount and constitutes the fenestrated elastic membrane of Henle. The media likewise is thicker, the increase,

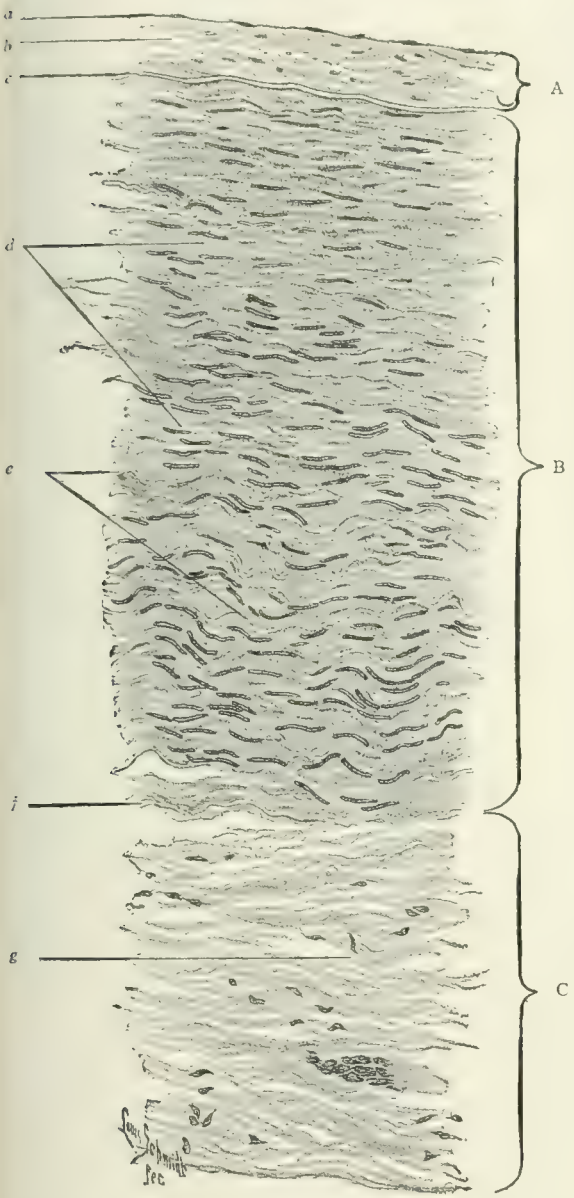

Fig. 822.—Section of Human Aorta. A, Intima; B, media; C, adventitia; *a*, endothelium; *b*, subendothelial tissue; *c*, internal elastic membrane; *d*, involuntary muscle; *e*, elastic tissue; *f*, external elastic membrane; *g*, fibroelastic tissue.

however, being due not so much to the greater amount of involuntary muscle as to the addition of fibroelastic tissue, which here bears a much greater proportion to the muscular tissue. This increase of fibroelastic tissue is responsible for the diminution of elasticity and the increased stiffness which characterize the walls of the larger arteries. The elastic tissue of the media in the latter vessels is often condensed to form an *external elastic membrane* (*f*), which defines the boundary between the media and the adventitia. The adventitia is also thicker, but the increase in this tunic is proportionately less than that affecting the intima and media. The adventitia of small arteries, in relation to the other two coats, is thicker than that of the large arteries.

The small arteries and arterioles, on the other hand, differ from the medium-sized vessels by a reduction in the thickness of their coats. The subendothelial tissue almost entirely disappears, while the involuntary muscle of the media is reduced to an attenuated layer of muscle cells, with little or no admixture of fibroelastic connective tissue. The adventitia consists of a few longitudinal bundles of fibrous tissue, with often an absence of elastic fibers.

Among the *structural peculiarities* of certain arteries may be mentioned the slight development, or even complete absence, of the subendothelial connective tissue in the celiac, the external iliac, the mesenteric, the renal, and the uterine arteries of young individuals. The aorta possesses a marked development of the subendothelial connective tissue, as well as the presence of longitudinal muscle cells within the intima. Longitudinally disposed muscle is present in the media of the subclavian artery and in the adventitia of the iliac, the superior mesenteric, the splenic, the renal, and the dorsalis penis, as well as in the umbilical arteries of the fetus. Some arteries, notably the vessels within the cranial cavity and the vertebral canal, possess coats which are very thin in proportion to their caliber. In these vessels, however, it is the media and the adventitia that suffer reduction, the intima remaining almost unaffected.

Capillaries.—The capillaries are microscopic vessels establishing communication between the arteries and the veins. In the tips of the fingers, the tips of the toes, the tip of the nose, the splenic pulp, and the erectile or cavernous tissue of the genital organs the

Fig. 823.—Capillary Blood-Vessels from Mesentery of Dog. × 240. 1, Capillary; 2, nuclei of endothelial plates; 3, connective-tissue cells.

arteries communicate directly with the veins. In the horny epithelium of skin and in cartilage, especially in the hyaline variety, no capillaries are present, while in the splenic pulp the existence of true capillaries is also doubted by most authorities. Minot suggests the name of sinusoids to the vascular spaces present in the erectile tissue, maternal placenta, coccygeal gland, parathyroids, and certain fetal tissues including the liver; in all of which vascular spaces are present that are comparable to the capillaries in structure, but not in diameter or extent.

A capillary (Fig. 823) consists of a single layer of

nucleated endothelial cells united by a small amount of intervening cement substance. By reason of the character of their thin walls, they are virtually protoplasmic tubes admirably adapted to facilitate the distribution of nutritive fluids to the tissues or, as in the pulmonary alveoli, to the interchange of gases. As the capillaries become larger a delicate tunica adventitia is superadded, which is formed of a delicate network of fine fibrils, composed of the processes of stellate cells lying directly upon the vascular walls. Each of these stellate cells consists of a large elongated nucleus, invested by an extremely delicate layer of protoplasm. The protoplasm of which the cells are composed is always more abundantly and distinctly granular toward the center and around the nucleus, while near the margin it is quite clear, and thins off to a delicate border. The capillaries by their union constitute the capillary plexuses, *retia capillaria*, which are more or less constant in the different organs. The forms presented in these plexuses depend to some extent upon the disposition of the elementary parts, and are also in some degree dependent upon the energy of the function. There are in many organs certain tissues into which vessels never penetrate—as the transversely striped muscular fiber, the nerve fibers, cells of all kinds, gland acini—and which, therefore, according to their form, trace out definite courses for the capillaries, so that they sometimes present elongated meshes, sometimes rounded, narrower, or wider reticulations.

The mode in which the capillaries pass into the larger vessels is interesting. On the arterial side it is found that the capillaries, as they become wider, present more closely placed nuclei, and are then invested externally with a structureless tunica adventitia and solitary muscle cells, the whole structure exhibiting the aspect of arterioles. On the venous side the transitionary vessels are less characteristic for a greater length. The first thing that is superadded, on this side, to the capillary wall is an external, homogeneous nucleated layer, which may be regarded as a sort of connective tissue—the tunica adventitia—forming a distinctly laminated structure, the venule. Besides the finest capillaries, which, however, always admit the passage of very flexible blood corpuscles, some observers have admitted the existence of still finer vessels, the so-called *vasa serosa*, which no longer allow of the passage of blood, but only of its plasma. Hyrtl thinks that it is necessary to admit of the existence of vessels of this kind in the cornea.

The Veins.—A typical vein, as shown in the accompanying drawing (Fig. 824) has thinner walls and a larger lumen than the corresponding artery; to this rule, however, the pulmonary veins are exceptions, since they are of the same capacity as, or of less capacity than, the pulmonary arteries. The constitution of the coats of a vein is less constant than it is in an artery, variations in the arrangement, proportion, and amount of the component tissues being very frequently encountered.

The *inner coat*, or *tunica intima*, consists of (*a*) endothelial cells, (*b*) subendothelial connective tissue, and (*c*) elastic fibers. The endothelium is composed of a single layer of cells held together by interstitial cement substance. The cells are shorter and wider than the corresponding lanceolated elements of the artery. The subendothelial connective tissue is very scanty in the majority of veins and rudimentary or even entirely absent in the smaller ones. The elastic tissue, often represented by a few longitudinal bundles, is less developed and does not form a fenestrated membrane.

The *middle coat*, or *tunica media*, is much thinner and looser than in the artery, chiefly on account of the admixture of connective tissue associated with the circularly disposed involuntary muscle cells. The elastic fibers, so conspicuous in the media of the artery, are very few in the vein.

The external coat, or tunica adventitia, is the thickest coat of the vein, reaching often twice or even three times the breadth of the media. It consists of wavy bundles of white fibrous tissue, usually following a circular direction, among which a few longitudinal fibers may be found; the greater number of the latter fibers are of the elastic variety. Connective-tissue cells are present in considerable number. The walls of the vein are nourished by vasa vasorum similar to those supplying the arteries.

Many veins, especially those of the lower extremities, are provided with valves; these are crescentic folds of the intima, which are brought into apposition by the dilatation of the pockets formed between the attached portion of the valve and the wall of the vessel. The valve consists of an extension and thickening of the fibroelastic tissue of the intima, covered on each side by endothelial cells. The free edge of the valve is thicker than the attached border.

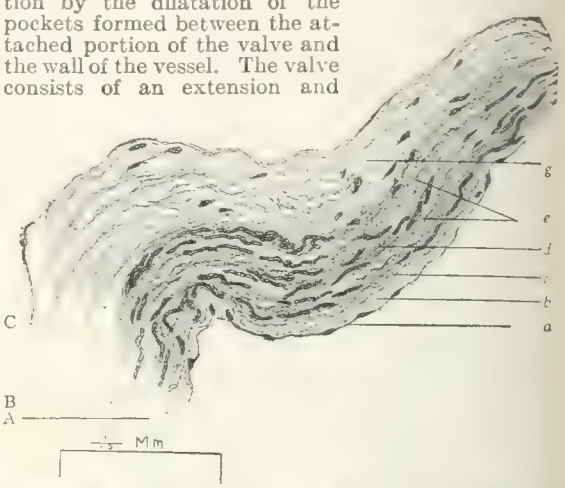

Fig. 824.—Secton of Human Radial vein. A, Intima; B, media; C, adventitia; *a*, endothelium; *b*, subendothelial tissue; *c*, internal elastic membrane; *d*, involuntary muscle; *e*, elastic tissue; *g*, fibroelastic tissue.

The variations in the structure of veins depend largely upon modifications of the muscular tissue. The involuntary muscle is best developed in the media of veins of the inferior extremities; in the veins of the gravid uterus involuntary muscle occurs in the adventitia as well as in the intima. Additional longitudinally disposed bundles of muscle are present in the inner part of the media in the mesenteric, the iliac, the femoral, and the umbilical veins. Involuntary muscle is sometimes encountered in the adventitia, in the abdominal cava, the axillary, the hepatic, the external iliac, the superior mesenteric, the renal, the splenic, the spermatic, and the azygos major veins. The presence of striated muscle in the pulmonary veins and cardiac ends of the vena cava is to be regarded as an extension of the striped muscular tissue of the auricular wall. Robert Formad.

Blood-vessels, Pathological Anatomy of the.—

The Capillaries.

The capillaries are less independent structures than the arteries and veins, and the pathological changes in the capillary wall are intimately connected with lesions in the surrounding tissues. The important rôle played by the capillaries in the different forms of inflammation is discussed in the article on *Inflammation*.

All tissue proliferation, whether inflammatory or non-inflammatory, is almost without exception associated with the new formation of capillary vessels by processes of budding of preexisting capillary endothelium, and these changes are described in the article on *Regeneration*.

The capillary angiomata and telangiectasias of congenital or acquired origin form mostly flat tumors of the skin and subcutaneous tissue, of a bright red color and a soft feel; the capillaries in them have thick cellular walls, and there is abundant evidence that new capillaries have been formed. Similar changes occur in capillaries in other tumors (see *Tumors*).

Long-continued congestion will result in dilatation of the capillaries, capillary ectasis or capillary aneurysm; this is shown well in passive congestion of the lungs.

Hyaline degeneration of the capillary walls is frequently observed in the brain, especially in paralytic dementia, but also in the kidney, the conjunctiva, the lymph glands, and in various tumors. Hyaline degeneration of the glomeruli is an important alteration in chronic nephritis, especially the interstitial form. In certain tumors mucoid degeneration of the capillary walls may take place.

Mallory in his study of colloid or hyaline changes in the brain shows that the material is always deposited in the vessels; in the larger vessels the middle coat is earliest and most affected. The hyaline material has a marked tendency to calcification, and in some cases the capillary network of the central cortex, the dentate nucleus, and the granular layer of the cerebellum undergoes hyaline change with calcification; this causes atrophy of the included nervous tissue and leads to the formation of sand-like deposits and of stone-like concretions.

Fatty changes in the capillary cells occur frequently, especially in the nervous system and in various toxic and infectious states. The lesions in the capillaries that may underlie the tendency to spontaneous hemorrhage in the hereditary and acquired hemorrhagic diathesis have not been cleared up; in these conditions it is difficult to determine whether the hemorrhages result from diapedesis or from rhexis. The relations of the capillaries to thrombosis and embolism are described in the articles dealing with those subjects.

Calcareous infiltration of the capillary walls occurs in the brain of old people; generally calcification is preceded by hyaline degeneration. Calcification of the capillaries also takes place in certain tumors, especially psammoma.

Amyloid degeneration is an important change in the capillary walls, observed always in the capillaries of the spleen, kidneys, liver, etc., in general amyloidosis. The amyloid material appears first in the delicate capillary sheath outside of the endothelium, which is soon crowded to one side, closing the lumen.

The Arteries and Veins.

Abnormalities.—Congenital abnormalities of blood-vessels may concern width, thickness of wall, origin, and course. Deviations from the normal in these respects on the part of the smaller and medium-sized vessels are considered to best advantage in connection with the normal anatomy of blood-vessels.

The congenital defects and anomalies of the *pulmonary artery* and *aorta* are closely associated with defects and anomalies of the heart. Among the important irregularities of the primary vessels is transposition of the aorta and the pulmonary artery. This may occur in hearts that are not otherwise defective or in association with developmental anomalies of the heart. Transposition of the venæ cavæ and the pulmonary vein may occur. In nearly all cases of this kind the foramen ovale is open to a greater or lesser extent and generally the ductus arteriosus is also pervious. Death occurs in early infancy.

The septum between the aorta and pulmonary artery may be defective. In an instance of this kind that I examined there was an oval defect about 1.5 centimeter in its greatest diameter between the pulmonary artery and the aorta, so that the beginning of the aorta and pulmonary artery had a common trunk from which emerged, in the usual places, the right and left pulmonary arteries and the branches of the arch of the aorta. The ductus arteriosus was patent and large, the aorta distal to the duct wider than that proximal to the duct. The foramen ovale was widely open. The large veins and the heart were normal.

Aortas with double arches occur. According to Lee Shaw, Hommel, in 1737, was the first to record this anomaly. In his case the two divisions united after encircling the trachea, and passed downward on the left side of the vertebral column. In another case (Malacarne) five valves guarded the aortic opening of the left ventricle and the arterial trunk immediately divided into two branches, which before uniting embraced the pulmonary artery, trachea, and esophagus; from each division was given off in succession a subclavian, an external, and an internal carotid artery. In Welch's case, the posterior branch passed between the trachea and esophagus, and from each division arose a common carotid and a subclavian artery. On the posterior branch was found an aneurysm from which the right common carotid took origin. Lee Shaw's specimen differs from all of those described except Malacarne's, in that the two divisions unite behind the esophagus. It differs from all in that the right branch is the larger, the junction of the two branches is on the right side, and the descending aorta passes downward on the right side, to the upper border of the eighth dorsal vertebra. This arrangement not only resembles the vascular arrangement in the reptile, but also more closely follows the distribution in the bird than it does that in the mammal.

Premature obliteration of the ductus arteriosus has been described as causing an abnormal smallness of the pulmonary artery. The pulmonary artery may divide at a point lower than usual, or arise by two distinct roots, instead of continuing into the aorta as the ductus arteriosus; it may form the left subclavian artery. Supplementary or vicarious branches distributed to the lungs may arise from the aorta as far down as the celiac axis.

In narrowing or obliteration of the aorta after having given off the vessels to the head and upper extremities, the inferior parts of the body are supplied with blood from the pulmonary artery through the ductus arteriosus; the descending aorta is said to be given off from the pulmonary artery. Now if the degree of constriction of the aorta be but slight at the time of birth, the ductus arteriosus may become closed. Later in life great narrowing and even complete obliteration of the aorta may take place (Fig. 825).

The theory usually offered in explanation of the pathogenesis of this condition was first broached by Skoda in 1855. The narrowing is made dependent upon the presence in the walls of the aorta of embryonal connective tissue connected with the ductus arteriosus; the postnatal involutional changes then lead to varying degrees of stenosis of the lumen of the aorta. Aberrant vestiges of duct tissue may occur in the aortic walls. Thombosis of the aorta beginning in the ductus arteriosus may end in complete aortic obliteration (Rauchfuss).

Of 113 cases of narrowing and closure of the aorta at or near the opening of the ductus arteriosus studied by Wadstein, atresia was present in twenty. In 16.4 per cent. the maximum narrowing was above the duct, in 33.8 per cent. on a level with the duct, and in 44.8 per cent. below it. The narrowing is sometimes double. In about a third of the cases the aorta was sclerotic, and generally more so on the proximal side of the narrowing. The most important secondary changes are hypertrophy of the left ventricle and the formation of collateral circulation, the blood reaching the lower portion of the body through the intercostals and the abdominal aorta, through the superficial

epigastric and long thoracic arteries and the deep epigastric, and through the anastomoses of the intercostals with the iliolumbar and circumflex iliac arteries.

The ductus arteriosus is as a rule completely obliterated within from one to two weeks post partum. The obliteration is accomplished by contraction and endarterial proliferation. The resulting scar in the wall of the aorta often becomes calcified. Incomplete involution of the ductus arteriosus may become the occasion for thrombosis; the thrombus may project into the aorta and into the pulmonary artery and give rise to embolism (Klob).

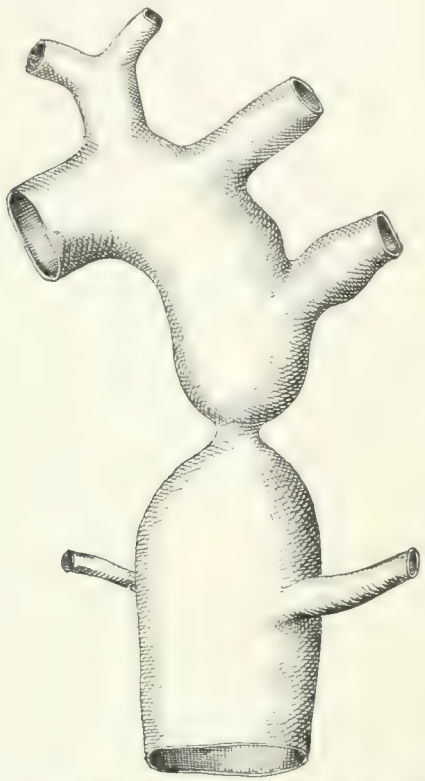

Fig. 825.—Stenosis of the Aorta at the Ductus Arteriosus (Modified from Cruveilhier.)

Transposition of the *large veins* occurs in connection with cardiac abnormities. There may be two ascending or two descending venæ cavæ, in the first case due to failure of union of the canals of Cuvier; less than or more than four pulmonary veins, which may be inserted into the superior vena cava, into the left innominate vein, or into the ventricles. Either of the venæ cavæ may be absent. An apparent reduplication of the inferior vena cava results from the union of the hepatic veins in one stem, which may empty into the vena cava above or below the diaphragm, or directly into the right auricle. The union of the iliac veins may take place higher than usual, the right and the left iliac vein continuing upward on each side of the aorta, sometimes as far up as the liver.

Coronary Arteries.—Abnormities of the coronary arteries have been described (Hepburn, Turner, Brooks, and others). The most frequent deviation from the normal is an increase in number and irregularities in branching. Brooks describes the origin of a coronary artery in the right anterior sinus of Valsalva of the pulmonary artery; this abnormal coronary anastomosed with the right coronary and acted as a vein owing to the greater pressure in the aorta. In another, more complicated case, Brooks found an artery originating in the beginning of the pulmonary artery, anastomosing with the aortic coronaries and the left subclavian artery; it entered into intimate relations with a cirsoid mass at the base of the pulmonary artery. This vessel also acted as a vein, emptying its blood into the pulmonary artery.

Aplasia or hypoplasia of an organ or part of the body is associated with absent or diminished development of the corresponding vessels. Abnormal origin and course of vessels are of greater surgical than clinical interest, because it is rare that such abnormalities cause symptoms. The origin of the right subclavian artery to the left of the left subclavian artery and its coursing in front of or behind the esophagus as it passes over to the right side may cause difficulties in swallowing, according to Eppinger. Differences in the size of the radial arteries and in the relative depths of their situation frequently give rise to apparent differences in the pulse on the strength of which the existence of aortic aneurysm, for instance, may be erroneously diagnosticated.

Vascular Hypoplasia.—Congenital smallness of the entire cardiovascular system is an interesting condition. The walls of the aorta are thin, the intima is the seat of wavy lines, and the lumen scarcely admits the little finger at a period when the aorta usually is twice or more as wide. The condition is frequently associated with arrested development of the reproductive organs and of the sexual characteristics of the body. Apparently the anomaly is more frequent in the female than in the male sex. Virchow urges that the arrest of development causes the chlorosis found in such cases but this explanation is not satisfactory. "That a disorder so common and for the most part so curable should depend upon a malformation so grave and so incurable as this aortic and general vascular hypoplasia is on the face of it highly improbable" (Clifford Allbutt). While hypoplasia of the aorta usually is associated with hypoplasia of the heart, the latter may be hypertrophied.

The developmental defects in the vessels in hemophilia are considered under the latter heading.

Retrogressive Changes in Blood-vessels.—*Atrophy.*—In chronic anemia and marasmus, senile and otherwise, simple atrophy takes place in the walls of the blood-vessels, especially in the muscular and elastic coats. Atrophy of individual organs is followed by or associated with atrophy of the corresponding vessels. When an extremity is removed the arteries and the veins that nourished the part decrease in size by an atrophy that may be called adaptive; the vessels become less and less until they carry no more blood than necessary for the nutrition of the remaining tissues (Fig. 826). In the beginning this adaptation is favored by contraction of the arteries and a little later by the development of new connective tissue in the intima, so that the lumen of the arteries is reduced in size. Similar processes occur in physiological atrophy seen in involution of the ductus arteriosus, the umbilical vessels, etc., the lumen closes and the elastic and muscular elements in the wall become replaced with connective tissue.

Fatty Changes.—Changes in the blood or disturbances of circulation may induce fatty changes in the walls of otherwise healthy blood-vessels, especially in the endothelial cells, the subendothelial layers, and the muscle cells of the arteries. Fatty changes are of common occurrence in arteriosclerosis. A vessel the seat of fatty change presents upon its surface opaque, white or yellowish-white patches and irregular lines, running longitudinally or forming a network, sometimes striated, sometimes of a uniform color. The surface is no longer smooth but velvety. These appearances are due to fatty granules and drops of fat in and between the endothelial cells. The change occurs also in the cells of capillaries. Cells may ac-

cumulate around and in areas of fatty change, taking up the oily detritus, and proliferation of cells also occurs.

Disintegration of the degenerated areas results in small defects ("fatty ulcers") which may become the starting point of thrombosis or traumatic and dissecting aneurysms; on supervention of trauma or severe strain the deeper layers of the intima are ruptured and the blood current makes its way between the layers of the wall. According to Paget fatty degeneration of the media is responsible for many instances of cerebral apoplexy. Fatty changes in the media are common in various intoxications and are frequently followed by calcareous infiltration.

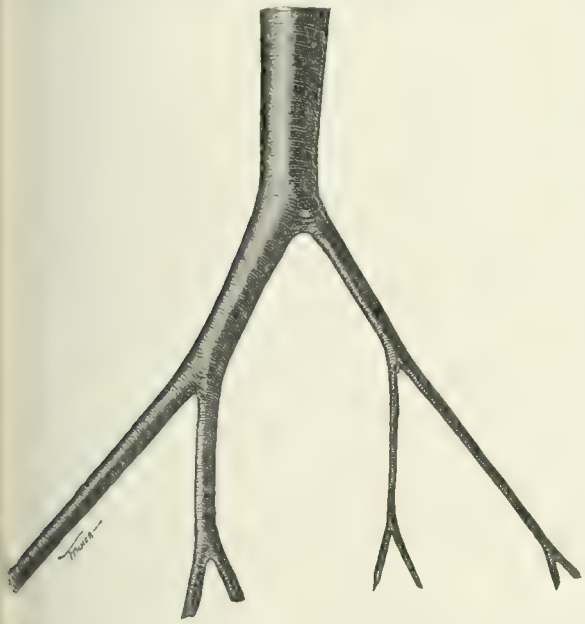

Fig. 826.—Atrophy of the Left Iliac Artery after Amputation of the Thigh. (Two-fifths natural size.)

Fatty changes occur most commonly in the aorta and the pulmonary artery, and then in the arterioles and capillaries, especially of the brain; the veins are not as frequently affected as the arteries.

Amyloid Degeneration.—The vascular system is especially prone to amyloid change, which takes its beginning in the media of the arterioles of parenchymatous organs. It also develops in the intima of the larger arteries, appearing as fine striæ and points, which are difficult to recognize with the naked eye unless first subjected to the action of Lugol's solution (see *Amyloid Degeneration*).

Hyaline Degeneration.—Hyaline degeneration of the smallest vessels and of capillaries is frequently observed in the spleen, the lymph glands, the renal glomeruli, and elsewhere. The endothelium, at first intact, is finally destroyed and the lumen narrowed and occluded. In larger vessels hyaline degeneration appears first in the intima, and it forms an early step in the complicated degeneration of arteriosclerosis. Hyaline material tends to become calcified. A good example of a hyaline degeneration of the muscular coat is seen in the pial arteries in tuberculous leptomeningitis.

Calcareous Infiltration.—Calcareous particles in glistening granules and as compact masses are frequently deposited in hyaline and fatty areas; it probably does not occur as an isolated primary process, and is most frequent and most extensive in senile arteriosclerosis. Gazert found that in a normal aorta the amount of earthy material is 0.43 per cent.; in a sclerotic and calcified aorta the calcareous material equalled 8.79 per cent. of the dry residue.

In old persons calcification may take place in the media of the arteries of the extremities; calcareous rings and tubes may form; usually fatty changes precede the calcareous deposition.

Metastatic calcification as a result of resorption in bone is said to involve especially the abdominal vessels, large calcareous plates forming which are separable from the surrounding tissues.

In some instances *true bone* has formed in the walls of arteries the seat of petrifaction.

Desquamation of the Endothelium.—In microscopic sections the epithelium of the vessels, both arteries and veins, is often found to have separated from the intima, the peculiar epithelial cells lying curled up in the lumen. This condition is not constant, and the peculiar circumstances under which it occurs have not been established. The loosened endothelial cells have been mistaken for sarcomatous emboli.

Hypertrophy and Hyperplasia.—Hypertrophy and hyperplasia of arteries are observed in connection with various forms of overgrowth, *e.g.* the uterus in pregnancy, large tumors, and the adaptive hypertrophy of one kidney in case of extensive disease or absence of the fellow kidney. Obstruction to the blood current and increased arterial tension, as in cases of hypertrophy of the heart and of chronic nephritis, produce more or less hypertrophy of the muscular coat of the arteries. The power of the arteries and veins to adapt themselves to new conditions is best shown by the changes that take place in the development of collateral circulation. Indeed, this is one of the richest fields for the study of pathological adaptation. Vessels and vascular systems adjust themselves with wonderful precision to changes in pressure, in velocity, and in quantity of circulating blood. Readjustment is accomplished by virtue of the vasomotor nervous mechanism and the physical properties of the arterial walls, aided under special conditions by structural changes. The physiological prototype of collateral circulation is seen in the changes that occur in the fetal circulation after birth. The ease with which the important rearrangements to the conditions of extrauterine life are accomplished indicates that the mechanisms for adaptive changes on the part of the circulatory system are good; as in almost all pathological adaptations, the mechanisms are in better working order in the young than in the adult and the old.

The extent of the changes incidental to the development of collateral circulation will depend naturally upon the location of the obstruction and upon the size and the number of the collateral branches. Formerly it was taught that the increased pressure above the obstruction was the cause of the development of collateral circulation; increased pressure is now regarded as a factor of little consequence. Nothnagel has shown that there is really no rise of pressure in the vessels above the obstruction or ligature unless they stand in communication with branches below the obstruction. As advanced by von Recklinghausen, the increase in the extent of the capillary bed of the collateral branches, through which the blood flows into the capillaries of the obstructed vessel, results in increased rapidity of the current; and Thoma claims that increased rapidity of the current is followed by a widening of the lumen of the vessels, increased thickness of the wall, and growth in length. In this way the need of the tissues for blood is satisfied. The structural changes that take place in the walls of the collaterals may be regarded as the expression of a work-hypertrophy. And conversely, the gradual thickening of the intima of the occluded vessel as far back as the nearest collaterals is to be regarded as the result of diminished need of work.

In obstruction to the portal circulation by cirrhosis of the liver the dilatation and hypertrophy of the veins through which collateral circulation is gradually established may become marked. In exceptional cases the esophageal veins become enlarged to many times their normal size and afford so complete escape for the portal blood that the congestions and the ascites of cirrhosis fail to appear and the clinical picture of the disease is masked.

Inflammation (Angiitis, Vasculitis).—Inflammation may affect principally the adventitia, the media, or the intima (periarteritis and periphlebitis, mesarteritis and mesoplebitis, endarteritis and endophlebitis). On account of the structure of the venous wall, these distinctions are not as marked in veins as in arteries. Angiitis may assume various types, such as productive, suppurative, tuberculous, and syphilitic. Angiitis may result from the extension of inflammatory processes in the neighborhood (consecutive angiitis); it may be caused by wounds of arteries or veins and by other forms of trauma, such as tearing and crushing (traumatic arteritis and phlebitis); it develops as a result of infections (pyogenic, syphilitic, and tuberculous) and of intoxications; in angiosclerosis arteritis and phlebitis are observed as consecutive processes, secondary to nutritive and mechanical disturbances in the vessel wall. Arteritis and phlebitis sustain a double relation to thrombosis inasmuch as thrombosis induces inflammation (thromboarteritis, thrombophlebitis) while angiitis not uncommonly leads to thrombosis. The causes of infectious or toxic angiitis may reach the part of the vascular wall first involved through either the vasa vasorum, the lymph stream, or the main blood stream within the lumen of the vessel, or they may come directly from without.

It was the custom of pathologists in the early part of this century to look upon imbibition and reddening of the tunica intima as evidences of acute inflammation; in 1847 Virchow proved the incorrectness of this view.

Because the same agent may produce more than one form of arteritis and phlebitis, and because the same form of angiitis may result from more than one cause, it becomes rather difficult to make at once a comprehensive yet simple classification of arteritis and phlebitis. When we omit from consideration periarteritis nodosa and the specifically tuberculous and syphilitic varieties, then the remaining forms belong to one of two large groups, the suppurative and destructive or the productive, the first characterized by disintegration and the formation of pus, the second by the production of new tissue.

Suppurative Angiitis; Suppurative Thromboarteritis.—The form of disease of the arterial wall induced by thrombosis or by the lodgment of emboli is determined by the nature of the thrombus or embolus. In the case that pyogenic bacteria are present in their interior, purulent inflammation is set up in the walls of the artery, resulting in a more or less extensive and destructive panarteritis and periarteritis, the final outcome being an abscess. This is what occurs in the development of metastatic embolic abscesses in the lungs. At other times the destructive action of the bacteria in infected emboli may be more limited in its extent, thereby producing a local weakening of the arterial wall, at which point aneurysmal bulging occurs and there results a so-called embolic or mycotic aneurysm (Goodhart, Eppinger). Mycotic embolism, the result of embolic suppurative arteritis, is observed most frequently in the cerebral arteries. Purulent thromboarteritis, with or without mycotic aneurysm, is liable to result in hemorrhage from the weakening and destruction of the vessel wall.

Suppurative Thrombophlebitis.—This may result from the extension of a suppurative process about a vein to the adventitia, media, and intima, which is more frequently the case than thrombosis upon the basis of a primary mycotic endophlebitis. In either case the resulting thrombosis undergoes purulent or purulent and putrid softening under the influence of the microbes that gain entrance into it from the walls of the vein. Beginning with John Hunter, in 1793, who described inflammation of the inner walls of veins after blood-letting and in the uterine and femoral veins of women in the puerperal period, it gradually became established clearly that pyemia commonly depends upon suppurative thrombophlebitis, the circulating blood being the medium of transference of infected particles from the thrombus to various parts of the body, the emboli on lodgment producing metastatic abscesses. Among veins that are liable to suppurative thrombophlebitis may be mentioned the umbilical veins in the new-born, infection taking place at the navel; the lateral and other sinuses of the dura mater in suppurative mastoiditis and middle-ear disease; the mesenteric veins in appendicitis and ulcerative processes in the intestines, the process giving rise by extension or embolism to suppurative pylephlebitis and abscesses of the liver; the subcutaneous veins in the vicinity of foci of infection, etc. Suppuration originating in a diverticulum of the esophagus has extended to the superior vena cava and given rise to suppurative thrombophlebitis in this vein.

Mycotic and Toxic Endangiitis.—Acute verrucose and ulcerative endangiitis, similar to acute endocarditis, most frequently occurs in the aorta and the pulmonary artery and is usually associated with endocarditis of the semilunar valves. It has also been described in the larger and medium-sized branches of the aorta and the pulmonary artery. The lesions usually assume the form of warty eminences, composed of a cellular and vascular granulation tissue and capped by thrombotic deposits. There is more or less cellular infiltration into the vessel wall near such warty outgrowths, and at times the process assumes more of an ulcerative and destructive type. Osler has described an instance of multiple mycotic aneurysms of the aorta the result of infective endaortitis associated with acute infective endocarditis, and the sudden development of aneurysms, one upon the radial artery and one upon the posterior tibial, in acute rheumatism, has been observed. Such aneurysms, although not embolic, belong etiologically in the same category as aneurysms caused by embolic destructive arteritis.

It is now recognized that acute and chronic forms of arteritis occur in various infectious diseases—typhoid fever, smallpox, scarlet fever, measles, acute articular rheumatism, influenza, pneumonia, syphilis, tuberculosis, and leprosy. In the acute forms cellular infiltrations, generally circumscribed, are found in the outer coats of the vessels together with more or less extensive proliferation of the subendothelial connective tissue of the intima. Nodular and more diffuse accumulations of lymphoid and epithelioid cells occur beneath the endothelium. These changes are explained as due to the circulation in the blood of the microbes and the toxic products of the diseases mentioned. When the endarterial changes result in destruction of the endothelium thrombosis takes place, and if it is in a larger vessel a typical verrucose endarteritis may be established. These changes occur probably more frequently in the veins than in the arteries. Arterial thrombosis in the diseases mentioned is often referable to infectious arteritis.

In many instances of multiple venous thrombosis it is not unlikely that an infectious or toxic endophlebitis is the primary change in the vessel wall. In typhoid fever, diphtheria, variola, influenza, and other infectious diseases there is found a nodular, sometimes a more diffuse, accumulation of lymphoid and endothelioid cells in the intima, even more frequently than in the arteries. Many of the large cells

in such foci seem to have marked phagocytic properties (Mallory). The accumulated cells, as well as the endothelium, may undergo necrosis and become the starting-point of a thrombus. Inasmuch as bacteria are often absent, it would seem that the vascular lesion may be caused by toxic products.

Lancereaux and others believe that there is a malarial aortitis which occurs in the form of gelatinous plaques, situated generally in the ascending part of the arch of the aorta; the lesion is described as beginning in the adventitia with cellular infiltrations which result in atrophy of the media and an adaptative thickening of the intima. Saccular aneurysms may result. There would be great difficulty in distinguishing between this malarial aortitis and nodular sclerosis from other causes.

Experimentally aortitis has been produced by the injection of various microbes—*B. typhosus, B. diphtheriæ*, streptococcus, pneumococcus, etc.—sometimes with and sometimes without previous traumatism to the artery by means of a probe inserted through the carotid. In some cases the lesions were vegetative, in others gelatinous plaques due to endarterial proliferation resulted. Infiltrations about the vasa vasis were often present. Nodular thickenings are described as following the injection of toxic substances, of lead, urate of soda, and phloridzin, with or without preceding injury. In their later stages the lesions might be identical with nodular arteriosclerosis.

Metastatic abscesses in the walls of arteries are rare. Virchow observed one in the beginning of the pulmonary artery; and Eppinger describes an abscess, the size of a walnut, in the posterior wall of the aorta just distal to the origin of the left subclavian artery.

Consecutive Exudative and Suppurative Angiitis.—While blood-vessels possess considerable resistance against the invasion of suppuration from without, so that in large abscesses it is not unusual to find the vessels wholly freed from the surrounding tissue and bathed in pus, yet periarterial and periphlebitic infiltration and proliferation are common consecutive lesions. This occurs in the vessels at the base of the heart in acute pericarditis, pleuritis, and mediastinitis; the adventitia is then the seat of an edema and infiltration. And suppurative and necrotic processes around blood-vessels may extend not to the adventitia only, but also to the media and the intima, causing necrosis of the endothelial lining and secondary thrombosis. In this way also may develop suppurative thromboarteritis and thrombophlebitis. The weakening of the wall of arteries caused by the purulent disintegration of the media sometimes results in another form of aneurysmal dilatation—erosion aneurysm produced by a kind of hernia of the inner coats at the point of least resistance. This result of consecutive peri- and mesarteritis is especially frequent in the branches of the pulmonary artery that are exposed upon the floor and the trabeculæ of phthisical cavities. The aneurysmal bulging takes place upon the side of the artery that is least supported by surrounding tissue, namely, that toward the lumen of the cavity. Frequently an obliterating thrombosis prevents the formation of aneurysm and removes the danger of hemorrhage under these conditions. Suppuration in a wound, or in an amputation stump, may destroy the granulation tissue formed by the intima in the process of definitive closure of an artery, cause purulent disintegration of any thrombus present, and thus give rise to the much-dreaded secondary hemorrhage of the preaseptic times.

Perforation of the inferior vena cava has been observed in amebic abscess of the liver.

On subsidence of acute inflammatory lesions of this nature, vascular granulation appears in the walls of the vessel, producing more or less extensive fibrous thickening of the various coats with narrowing of the lumen; in case thrombosis has taken place, the substitution of the thrombus by connective tissue may cause occlusion of the vessel. Terminal fibrous changes of this kind do not differ microscopically from the lesions of many primarily productive forms of angiitis.

Productive Angiitis.—Inflammation of blood-vessels resulting in the production of new tissue is frequent. In productive or obliterating endarteritis and endophlebitis there occurs a proliferation of the intima, which leads to thickening, eccentric narrowing of the lumen, and perhaps to complete occlusion. This process is observed under a variety of conditions. The occlusion after birth of the ductus arteriosus and the umbilical vein and arteries is accomplished by the formation of connective tissue by the intima; as the pressure of the blood in these vessels fails, a degree of contraction ensues that favors the filling of the vasa vasorum; in the narrowed lumen a small thread-like thrombus may form which is finally substituted by fibrous tissue. Similar changes occur in occlusion following ligature, and in the narrowing of the lumen of vessels the capillary bed of which has been restricted (amputations, indurative processes in the lungs, etc.). In these conditions there is usually atrophy of the media. A ligated vessel may be occluded by intimal proliferation without thrombosis taking place; in many cases a thrombus forms, which is then replaced by granulation tissue. In the old and feeble, especially when the arteries are sclerotic, the intima may have lost its power of proliferating and then there is danger of secondary hemorrhage.

Productive Thromboarteritis.—The presence in an artery of a thrombus, whatever the cause of the thrombosis, or of an embolus, is sooner or later followed by reactive changes on the part of the vessel wall, which result in the production of a vascular granulation tissue, provided destructive infection does not occur. The plug becomes infiltrated with phagocytes and with fibroblasts. The amount of new tissue and the rapidity with which it is formed will depend more or less upon the age of the patient and upon the previous condition of the walls of the artery in question. The vessels of the aged, the walls of aneurysms and of sclerotic arteries are often so changed and degenerated that but slight or no reactive proliferation takes place under conditions that in young healthy arteries are followed by vigorous growth of new tissue. The vessels present in the new tissue result in part from ingrowths from the vaso vasorum, in part from the endothelial cells of the intima. In case the lumen of the artery is but partially occluded, then the tissue replacing the thrombus or embolus gives rise to various forms of flattened elevations, projecting ridges and bands, cord-like networks. Complete occlusion of the artery may be followed by cicatricial obliteration of the lumen, or the new tissue may be so traversed by vascular spaces that the continuity of the lumen in some measure is restored. (For further details concerning connective-tissue substitution of thrombi, see article on *Circulation, Pathology of the.*)

In the healing of wounds of arteries and veins a thrombus composed of blood plates and of fibrin first forms, which is subsequently replaced by new fibrous tissue.

Productive Thrombophlebitis.—Productive inflammatory changes occur in the walls of veins after thrombosis. The process pursues the same general course as thromboarteritis. It is observed especially in the periuterine veins, the veins of the lower extremities, the pelvic veins, and the sinuses of the dura, which constitute those parts of the venous system that are most frequently the seat of thrombosis. The residues of connective-tissue replacement of a venous thrombus may be fibrous bands coursing across the lumen, the interior of the vein resembling that of a dural sinus, more diffuse intimal thickenings, and great shrinking of the part of the vein involved, with complete oblitera-

tion of the lumen. Such changes may occur also in the larger veins, such as the venæ cavæ.

Obliterating Endophlebitis of the Hepatic Veins.—An obliterating, proliferative phlebitis occurs in the main stems of the hepatic veins. This process has recently been studied by Chiari. In seven cases collected by him there were periphlebitic proliferative processes or thrombosis followed by productive thrombophlebitis. He describes three instances of an apparently primary obliterating phlebitis of the main stems of this vein, which on account of the resulting circulatory disturbances became the cause of death. The endophlebitic process was situated in the proximal portions of the veins with peripheral extension in one case. The tendency to obliteration was marked, leading to mechanical obstruction and fateful secondary thrombosis. The condition is undoubtedly a peculiar one, possibly of syphilitic origin; in one case it was associated with similar changes in the coronary arteries.

Consecutive Productive Angiitis.—Inflammation, acute and chronic, generally takes place in the walls of all arteries that lie in tissue the seat of inflammatory processes. In this case cellular infiltration and proliferation extend into the vessel wall from without inward, and all the coats may in time become fibrous; the thickening of the intima is generally pronounced and complete obliteration of the lumen may take place. In many instances the formation of fibrous tissue in the intima of vessels in organs the seat of chronic fibrous processes in some measure may be the result also of obliteration of portions of the capillary districts of the vessels (Thoma), the resulting narrowing of the lumen partaking of an adaptative nature. Changes of this character are seen in chronic interstitial inflammations and fibrotic processes in the parenchymatous organs, as in interstitial nephritis, orchitis, etc. (Fig. 827). They are well marked in

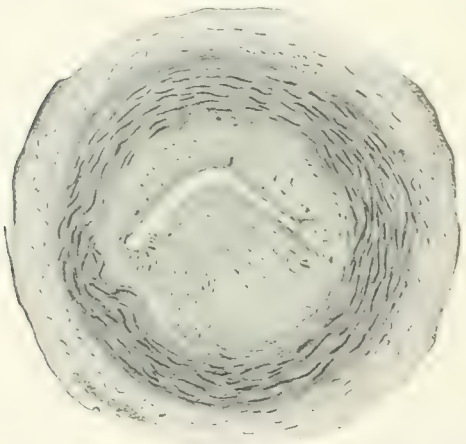

Fig. 827.—Obliterating Endarteritis in Chronic Salpingitis. (Hematoxylin and eosin. × 100.

the specific granulomatous processes, and the resulting arterial lesions need not necessarily present any specific characteristics. The acute stages can be studied nicely in the pial arteries in tuberculous leptomeningitis. There is leucocytic infiltration of the adventitia, extending into the media and intima; the cells are seen making their way between the fibers of the media and through the fenestrations of the internal elastic coat, the nuclei being drawn out long so as to pass through narrow spaces; the elastic coat at times becomes broken through by the cells which may accumulate under the epithelium; simultaneously fibroblasts appear, especially in the subendothelial layers (Fig. 828). Similar changes of a more chronic but nonspecific character are seen also in the walls of arteries and veins in chronic tuberculous areas and cavities in the lungs. Great narrowing of the lumen and even closure may result from the newly formed fibrous tissue in the intima. Quite similar changes occur in syphilitic lesions, and it is probable that an isolated, primary, histologically non-specific, productive endarteritis is often caused by syphilis. In productive endarteritis of whatever cause, fibrillar connective tissue interspersed with elastic elements is formed in the intima. At times a distinct, new, elastic membrane develops; it is generally thinner than the original elastic layer, the general course of which it imitates, and it forms the inner boundary of the new, greatly narrowed lumen. But the process is not thereby brought to a standstill, as new fibrous tissue may again form and completely occlude the vessel.

The perivascular changes that develop in connection with productive angiitis of diffuse character lead to obliteration of the perivascular lymph spaces and obstruction of the lymph flow, which in some tissues, as for instance the brain, may produce disturbances of the function and the structure.

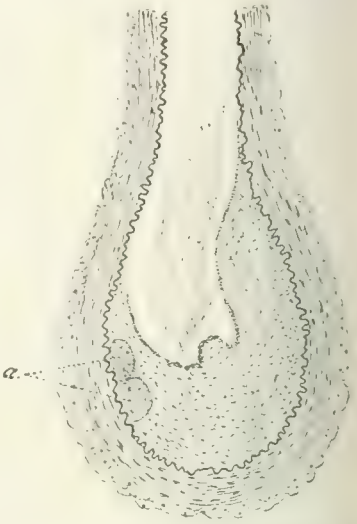

Fig. 828.—Chronic Endarteritis in Chronic Tuberculous Meningitis. *a*, Blood-spaces. × 150.

Acute endarteritis in time may give rise to fibrous nodules upon the intima and to diffuse thickening. Fenger describes an extensive polypoid fibrous endarteritis of the pulmonary artery associated with valvular endocarditis. The polypoid outgrowths, which almost closed the lumen, sprang from the deeper layers of the intima.

Elastic Fibers in Endarterial Proliferations.—The methods of staining elastic fibers have resulted in the demonstration that they are present to a greater extent in the endarteritic proliferations than was formerly thought. In arteriosclerosis the newly formed elastic fibers in the intima have the same general course as the fibers of the media (see Fig. 829). Jores holds that elastic fibers are formed in two ways: the one is due to the splitting up of the internal elastic layer into several lamellæ, some of which may appear as quite independent bands. This process occurs especially in arteriosclerosis and probably to some extent under normal conditions. But the new formation of fine fibers is by far the most important. Jores favors the theory that these fibers are formed by the secretory activity of the young connective-tissue cells, although it cannot be said that the origin of elastic elements from chemical changes in the collagenous intercellular substances has been wholly disproved. In intimal proliferations Weigert's elastic-fiber stain shows that the new fibers appear first as finer granular lines that surround the cells as a fine network. The endothelial cells do not seem to play any part in this process, inasmuch as elastic fibers never appear between the individual endothelial cells, but are always confined to the subendothelial layers. From observations on ligated vessels Jores found that new elastic fibers are formed more numerously in vessels subjected to the pressure of the circulating blood than in parts enclosed between two ligatures

or in vessels the seat of thromboarteritis. Hence he regards the new formation of elastic fibers as compensatory in character.

Obliterating Endarteritis and Spontaneous Gangrene.—The occurrence of obliterating endarteritis in an independent, primary form has not been established upon a satisfactory basis. Its occurrence as a secondary process in indurative processes, in the organization of thrombi, and as the result of consecutive and specific arteritis is generally recognized. Heubner interpreted endarteritis of the cerebral vessels as always a specific syphilitic lesion, but Baumgarten insists that not endarteritis obliterans is the specific form of syphilitic vascular disease, but gummous arteritis, in which the changes in the adventitia are equally if not more prominent than those in the intima. The endarteritis obliterans observed as the cause of spontaneous gangrene in the middle-aged and the young is regarded by many as a distinct and primary disease. This opinion is based largely upon the fact that premonitory symptoms, indicative of gradual occlusion of the arteries, may exist a long time before culminating in gangrene, the more prominent symptoms being pain, cyanosis, and coldness. In some cases the complex of symptoms called by Charcot "intermittent claudication" has been present. The arteries more frequently involved are those of the foot, leg, and forearm. The endarteritis, which is described as typical, with vascularization of the new tissue in the intima and reduplication of the elastic coat, begins in the peripheral branches. The adventitia may be greatly thickened, and in some cases the neighboring

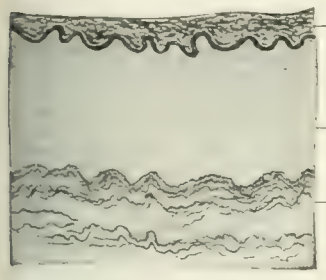

Fig. 829.—Diffuse Arteriosclerosis. Renal artery. Weigert's elastic-fiber stain. I, Intima with new elastic fibers; M, media, the seat of hyaline degeneration: no elastic elements; A, adventitia with increased number of elastic fibers. × 150.

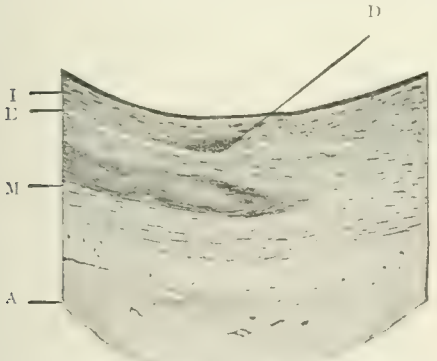

Fig. 830.—Sclerosis of Anterior Tibial Artery. Gangrene of foot from thrombosis. I, Fibrous intima; E, elastic lamina; M, media with hyaline degeneration and calcification; A, adventitia; D, beginning degeneration in intimal thickening. Hematoxylin and eosin. × 100.

veins and nerves were found extensively involved in the perivascular sclerosis. In many cases thrombosis or pigmentation, the probable result of thrombosis, was present, and Thoma, who does not believe there is a special form of obliterating endarteritis, holds that the endarteritic changes in this form of gangrene result from the replacement by connective tissue of thrombi in sclerotic vessels. Others hold similar views. Goebel attributed spontaneous gangrene in a child, one and a half years old, to thrombosis at the bifurcation of the popliteal artery produced by the presence of small globular elevations composed largely of elastic elements and caused by a local endarteritis of obscure origin. The conditions that may produce spontaneous gangrene not caused either by embolism and secondary thrombosis or by arteriosclerosis and thrombosis are consequently rather complicated. Undoubtedly many instances result from arterial thrombosis secondary to the endarterial inflammatory changes that occur in various infectious diseases (see *Gangrene*).

Angiosclerosis.—*Definition.*—Angiosclerosis is a complex process that appears under different conditions, in varying stages, and with varying distribution. The general idea conveyed by the term is fibrous thickening and other changes in the intima together with alterations of a degenerative nature in the media of arteries and veins. When the process affects arteries, and that is by far its more prominent, more important, and more frequent localization, it is arteriosclerosis; sclerotic changes in veins constitute phlebosclerosis. The changes of sclerosis in the aorta and larger vessels are described clearly by Morgagni and their relation to sudden death and to other results were recognized in the early parts of the nineteenth century. The term arteriosclerosis was introduced by Lobstein over fifty years ago and has come into more general use than the terms endarteritis chronica deformans s. nodosa (Virchow), and arteriocapillary fibrosis used by Gull and Sutton in their important paper on the relation of contracted kidney to arterial changes (1872). Atheroma is used sometimes as synonymous with arteriosclerosis, but is more strictly applicable to late changes of the process in the aorta and large branches in old persons.

Theories as to Genesis.—Through the work of Thoma especially, angiosclerosis, in some of the phases of its genesis, was placed upon the same basis as certain processes that occur in the vessels, especially the arteries, under physiological conditions.

The physiological paradigm of angiosclerosis was seen in the changes that take place in the aorta immediately after birth. At birth there is no connective tissue in the intima of the aorta. Immediately after birth the circulation in the umbilical arteries ceases; a part of the territory of the aorta is cut away, the aorta is now too large in comparison with the area it supplies with blood, and the circulation in it becomes slower. Under these circumstances connective tissue develops in the intima of the aorta, and in this way its lumen is reduced to a size commensurate with the rate of blood current best suited to the needs of the tissues. Later in life similar changes are said to occur in the carotid, for instance, because from the eighth to the tenth year the growth in strength of this artery does not keep pace with that of other vessels; hence it dilates, its lumen becomes so large that slowing of the circulation takes place, and new tissue develops in the intima until the current reaches the normal flow. Similar changes are believed to take place in arteries after amputation and in arteries whose capillary area is destroyed by disease. The connective-tissue formation in these cases is compensatory, calculated to reduce the lumens of the arteries to proper size.

From these and other observations the general theory was deduced that slowing of the blood current not completely remedied by a proportionate contraction of the media, leads to a new growth of connective tissue in the intima, which narrows the lumen of the affected vessel, and restores the normal swiftness of the current more or less completely (Peabody), the compensating endarteritis being regarded as the result of mechanical and chemical

changes in the intima. Klotz and others, however, hold that the theory of compensatory intimal hyperplasia cannot be maintained and that proliferative changes in the intima are not uniformly secondary to weakening of the media, but the result not of one but of many factors which act on both intima and media at the same time.

Histogenesis.—The principal change in the media in arteriosclerosis is a granular disintegration of the elastic fibers, which begins first in the inner parts of the media in the network between the elastic lamellæ. Later, changes appear in the lamellæ, which break up into irregular pieces. The chemical nature of the elastic elements changes in some way and they become basophilous. These are the earliest changes in the vessels and occur especially in advancing years. At the same time nodules or more diffuse thickenings appear in the intima, composed of fibrous tissue and new elastic elements arranged either as lamellæ or as networks of fine elastic fibers; this new formation easily undergoes degeneration (atheromatous changes), so that in arteriosclerosis there is degeneration of and new formation of elastic fibers. Foci of inflammation and proliferation in the adventitia and the media also lead to destruction of the elastic fibers in their vicinity. Periarterial and mesarterial inflammatory infiltrations about the vasa vasorum were regarded as of great importance by Köster and others. The etiology of such foci is probably to be sought in toxic and infectious influences. Certain French writers go so far as to advocate that the degenerative (atheromatous) changes in the large arteries are the result of sclerosis of the vasa vasorum.

At all events the new tissue in sclerosis is not able to maintain its integrity in the face of the constant strain of the intravascular pressure and of the inadequate nutrition. Hyaline and fatty changes take place in the deeper layers of the intimal thickening and in the inner layers of the media. Complete disintegration into fatty and granular débris mixed with cholesterin tablets and crystals of fatty acids gives rise to smaller and larger foci of softening often termed "atheromatous abscesses." By extension the overlying tissue may be destroyed, and defects arise in the intima—"atheromatous ulcers"—upon the rough surface of which fibrin may be deposited. Petrifaction often takes place in the degenerated tissue and calcareous plates and irregular masses form in the intima and inner layers of the media. True bony tissue also may develop. It is to this degenerative stage of sclerosis, which is seen best in the aorta and its larger branches, that the term atheroma is frequently applied. In advanced cases the sclerotic, degenerative, and petrifying changes are present in varying degrees and produce great deformity, unevenness, and changes in the normal color of the intima and irregular dilatations of the vessels. The relation of arteriosclerosis to aneurysm and of phlebosclerosis to varicosity of the veins is elaborated under those headings.

Etiology.—The etiological relations of angiosclerosis are ill defined. According to Edgren's statistics, syphilis, alcoholism, and old age are the predominating factors in the production of arteriosclerosis. Henschen points out that the source of the material for such studies must be carefully scrutinized because conclusions based upon the presence of arteriosclerosis in the inmates of institutions that harbor especially syphilitics, alcoholics, or old people naturally are misleading. Such studies usually have taken no note of the form of arteriosclerosis present.

Angiosclerosis in advanced years is so common that it is generally regarded as a sort of involutional change; this is true especially of the senile form. According to Thoma a moderate degree of thickening of the intima is frequent after the thirty-sixth year, especially in the peripheral arteries, and this statement is surely in harmony with the observations of pathologists in general.

The period of life at which a well-marked arteriosclerosis appears and the extent that it may assume are believed to be dependent upon the natural resisting power of the arterial wall and upon the amount of wear and tear to which the vessels are subjected. "A man is as old as his arteries." The tendency seen in certain families to the early development of arteriosclerosis is explained as due, at least in part, to an inherited weakness of the arterial walls. This theoretical conclusion has received as yet no confirmation in the form of demonstrable anatomical deviations from the normal in the structure of the arteries of such individuals. On the other hand, there are rare cases recorded in the literature of centenarians with smooth and normal vessels.

Numerous instances have been recorded of arteriosclerosis in children and young persons and it would seem very doubtful whether the sclerotic changes here depend upon a general primary weakening and loss of elasticity and contractility of the media. Special toxic and infectious influences may be at work in such cases, the sclerosis being the result of inflammatory and other lesions in the media.

Sratistics seem to show that men are more frequently affected with advanced angiosclerosis than women. Edgren's statistics give twenty-one per cent. of arteriosclerosis in women and seventy-nine per cent. in men. Arteriosclerosis apparently develops later in life in women than in men. This is ascribed to the fact that women live quieter and with less stress and strain than men.

Chronic intoxications and infections of various kinds are regarded as playing an important part in the etiology of angiosclerosis, but so far it has not been possible to make any etiological subdivisions of the disease. Among the intoxications those due to alcohol, lead, and gout are regarded as of the first importance. Tobacco is regarded by clinicians as not entirely free from deleterious action upon the arteries; Huchard thinks it exercises a special influence upon the coronary arteries. The precise mode of action of these substances can hardly be more definitely specified than that under the toxic influences degenerative changes develop in the arterial wall, especially the media. Tea and coffee have been accused of causing arteriosclerosis, but there is no evidence that they do so.

Infectious diseases in general appear to exercise a harmful influence upon the muscular and elastic parts of the walls of blood-vessels. Evidences of arterial changes are present in a large percentage of the bodies of children dead of acute infections. The closure of the vasa vasorum by inflammatory changes in the adventitia and the outer layers of the media would surely interfere with the proper nutrition of the inner layers of the wall. Of the chronic infections syphilis is the most important (see Syphilis of the Vessels).

The overfilling of the vascular system due to excessive eating and drinking and the increased pressure and strain upon the arteries in muscular work constitute another group of causes. According to Huchard and Edgren arteriosclerosis is inseparably connected with the pathogenesis of increased pressure. The relation of angiosclerosis to the intravascular pressure is seen in the distribution of the disease in the vascular system.

Arteriosclerosis sustains a double relation to renal disease. An existing sclerosis of the renal and peripheral arteries may interfere with the nutrition of the renal parenchyma to a degree that parenchymatous degeneration and connective-tissue overgrowth result. On the other hand, a primary interstitial nephritis by raising arterial pressure or in other ways may lead to connective-tissue growth in the intima.

Osler summarizes our conceptions of the etiology of arteriosclerosis as follows: "Etiologically, then, there

are three great groups of arteriosclerosis: first, the involutionary, in which the degeneration is caused by the ordinary wear and tear of life, and which is as natural as gray hair and failing eyesight; secondly, the toxic group, in which the degenerations are caused directly by the poisons of acute and chronic infections and of the intoxications; thirdly, the hyperpietic group, in which the degeneration follows persistent high arterial tension. Practically in a given case of arteriosclerosis, in a man of, say, fifty-five, two or all three of these factors may be present, and it is exceedingly difficult to assign to each their relative value."

Experimentally sclerotic changes have been produced by the injection of bacteria and bacterial toxins. Changes in the intima of a productive nature have been obtained after injections of typhoid bacilli and of streptococci and other bacteria (Klotz, Saltykow), while injections of diphtheria toxin have caused changes in the media. Adrenalin produces medial degenerations followed by calcification (Mönckeberg's sclerosis, the form usually present in the radials in clinical arteriosclerosis).

The Forms of Arteriosclerosis.—There is some confusion in the classification of arteriosclerosis. The various anatomical forms often are found connected by transitional stages. Thoma recognized two main forms, diffuse or secondary, nodular or primary. The former he regarded as due mainly to primary changes in the peripheral vessels and the capillaries and as consecutive to the increased peripheral resistance. The latter he regarded as the result of primary changes of a degenerative nature in the media, and as localized especially in those regions where the pulse wave is high and strong. Councilman holds that the diffuse form is a distinct disease associated with widespread changes in the media, and he distinguished a third form, the senile arteriosclerosis, in which the lesions are mainly degenerative, hyperplasia in the intima being but little marked.

Senile Arteriosclerosis.—In this form the process is largely one of degeneration and calcification with but little thickening in the intima. It represents the general atrophy and degeneration of senility as they affect the arteries when even connective tissue has lost much of its power of proliferation. In this form the heart is not always hypertrophied; atrophy of internal organs may be marked. The aorta and its larger branches are dilated irregularly, tortuous and elongated, the walls in general thinner than normal, stiff, and covered by calcareous plates or the seat of cavities containing grayish-yellow, grumous material —the detritus of degenerated, necrotic muscular and fibrous tissue. The cavities are sometimes called atheromatous abscesses; frequently the thin internal membrane is ruptured and rough spots and areas arise ("atheromatous ulcers") in the floor of which calcification may take place or thrombotic material accumulate. In typical cases the aorta and other large vessels are changed into rigid calcareous tubes, the inner surface being rough, frequently fissured, and covered by fibrinous masses. The intima has lost its glistening appearance.

The relations of senile arteriosclerosis to thrombosis, senile gangrene, cerebral softening, and other consecutive changes in the body are discussed fully elsewhere.

Diffuse Arteriosclerosis.—Here the lesions are widely distributed, embracing all the arteries of the body. The subjects of diffuse arteriosclerosis are generally in the prime of life. In twenty-seven cases studied by Councilman, the youngest, a negro, gave his age as twenty-three; the oldest was sixty. Most of the cases ranged between forty and forty-five; fourteen were white and thirteen colored. The negro seems disposed to this disease. Most of the subjects who come to autopsy are strongly built, well-nourished, muscular individuals. Heart hypertrophy is always present and may reach an extreme degree. In two of Councilman's cases in which there were no valvular lesions whatever, the heart in one weighed 850, and in the other 820 grams. The average weight was over 400 grams. Close examination often shows some degree of fibrous myocarditis, this depending on the degree of involvement of the coronary arteries in the general trouble. The cardiac hypertrophy may be confined to the left ventricle, but in most cases it is always associated with so much dilatation that the right ventricle also becomes hypertrophied. The dilatation may affect the integrity of all the valves. Anatomical lesions of the valves are usually absent. There may be some extension of the aortic disease to the aortic valves or to the aortic segment of the mitral valve, but the thickening so produced is not generally sufficient to interfere with the functions of the valves. The most marked changes are found in the aorta and the large arteries given off from this. The large arteries are more or less dilated, the dilatation in some cases starting in the aortic orifice and extending throughout the aorta and large arteries. The branches of the arch are sometimes relatively more dilated than the aorta. There is elongation of the vessels as well. The aorta makes lateral curves and the normal curves of other arteries are greatly accentuated. In addition to the dilatation there is a general diffuse thickening of the arteries, which is often relatively greater in arteries the size of the radial than in the large vessels. In the large arteries the intima is roughened by projecting elevations, which are frequently distinguished by differences in color and consistency. They may be of a pearly, transparent color and very hard, in both color and consistency similar to cartilage. They may be of an opaque, whitish-yellow color, and the center soft and pultaceous. On incising such places a soft, white, mortar-like mass may appear. We may find irregular, ragged excavations, often covered with fibrin, showing that the softening has extended through the intima of the vessel during life. Similar areas of softening and degeneration may be found in the diffusely thickened intima. There may be more or less calcification which is usually confined to the projecting elevations, but this never reaches the same extent here as in the senile form. There are frequently longitudinal folds and puckering of the intima as though due to the contraction of the vessel after death.

The two essential alterations are various degenerative changes in the media and a growth of tissue in the intima. The degenerations in the media are shown in various ways. Sections of the fresh artery show some fatty degeneration, but this does not play the chief part. The most common change seems to be necrosis and hyaline degeneration (Figs. 829 and 830). The muscle cells lose their nuclei and the whole muscular coat is changed into a homogeneous mass. The elastic fibers between the muscle laminæ are frequently broken up and disappear; these changes probably appear early in the process. In some sections of the dilated carotid, for instance, the media as such may not be recognized, the whole artery being changed into a dense, thick mass of sclerosed connective tissue. The tissue composing the intima consists of thick layers of dense connective tissue, which is prone to degenerative changes. The tendency to degenerative changes, however, is not so marked here as it is in the senile form.

This diffuse arteriosclerosis agrees best with the form which Thoma has described as secondary arteriosclerosis, and in which he considers that the changes in the large arteries are due to the resistance to the circulation that the diseased small arteries cause. In a paper on the conditions of the vessels in Bright's disease, Thoma holds that there is an opposition to the passage of the blood, which is due primarily not to a narrowing of the caliber of the vessels by the thickening of the intima, but to an increased permeability of the vessel walls. With this disease of

the vessels there is an increase in the connective tissue and destruction of large numbers of capillaries, still further diminishing the size of the vascular bed, and then comes a disparity between the caliber of the artery and the territory to be supplied, followed by a compensating growth of connective tissue. Councilman would rather take the view that the changes in the aorta and in the minute arteries are due to the same cause; that diffuse endarteritis is a disease primarily due to a degeneration of the muscular fibers of the media. On this the growth of the intima follows, which is due to the same cause acting in two ways: in one, by the well-known law of connective-tissue growth, to supply a defect, in this case the degeneration of the media; and in the other, possibly acting under the law of Thoma, a compensating endarteritis to restore the abnormally dilated vessel to a normal caliber.

Nodular Arteriosclerosis.—In the nodular or primary form of arteriosclerosis there are flat, button-like, hemispherical, yellowish or yellowish-white projections above the intima, especially about the orifices of the arterial branches. This is generally regarded as the result of the greater strain that this part of the artery is exposed to. The areas consist of new connective tissue and new elastic fibers in the intima, the underlying media being either fibrous, calcareous, or degenerated and necrotic. Thoma claimed that the cast after filling the vessel with melted paraffin injected under the same pressure as that of the blood came out smooth, showing that in the tense vessel the intimal nodules fill defects in the media. Klotz was not able to confirm this result. The weakening in the wall is liable to result in aneurysm (Fig. 831).

Fig. 831.—Nodular Sclerosis of Aorta with Beginning Aneurysm. Hematoxylin and Weigert's elastic-fiber stain. The intima (I) is thickened, contains parallel, wavy, elastic fibers, except at the point of the bulging; the media (M) is thinned, degenerated, the elastic broken up; A, adventitia. × 150.

The new tissue soon becomes hyaline, fatty changes take place, and eventually disintegration into fat drops, cholesterin, granular detritus gives rise to softening. The degeneration begins in the outer layers of the sclerotic thickening, but may extend inward until the epithelium lining the vessel is destroyed and a larger or smaller rough area due to loss of substance is formed. Calcareous infiltration may take place. More or less leucocytic and round-cell infiltrations occur around softened areas. The adventitia may be unchanged, fibrous, or the seat of foci of cell accumulations.

This form is possibly due to local, circumscribed areas of degeneration and weakening in the media produced by strain, by toxic and infectious lesions. Several investigators have produced apparently similar plaques in the aorta of animals by injection into the circulation of bacteria, bacterial toxins, and other substances, such as lead, etc., with or without producing traumatic lesions of the vessel wall. In some cases of this kind the lesions seemed to be the result of proliferation in the intima; in others there were mesarterial and periarterial inflammatory foci about the vasa vasorum.

In goiter of all forms, Jones found degenerative and sclerotic changes in the arteries of the thyroid and its capsule. The changes occurred apart from general arteriosclerosis. The vessels were abnormally friable. The internal elastic coat was granular, broken across, and calcified; in one case it had changed into a calcareous plate; connective-tissue thickening of the intima associated with the formation of new elastic fibers had resulted, followed by hyaline degeneration.

The Distribution of Angiosclerosis.—The relative frequency of angiosclerosis in the different parts of the circulatory system has been studied by Bregmann, Sack, and others. The arteries are more frequently involved than the veins, although the study of phlebosclerosis has been rather insignificant as compared with the amount of attention paid to arteriosclerosis.

Arteriosclerosis in general is more frequent in the vessels of the extremities than in the aorta and its branches of the first and second order; it is most frequent in the arteries of the leg and forearm, beginning first of all in the anterior tibial. This is explained on the score of the lateral pressure to which these vessels are exposed on account of posture in addition to the general hydrodynamic pressure. Sclerosis is often

Bregmann's Table Showing Relative Frequency of Arteriosclerosis in Different Arteries. The Figures Represent Percentages.

Normal.		Slight degree.		Medium degree.		Severe degree.		Without distinction in degree.	
Brachial	45	Radial	56	Carotid, internal	48	Aorta, abdominal	16	Ulnar	94
Iliac, external	42	Carotid, external	56	Subclavian	47	Cerebral	15	Tibial, anterior	92
Aorta, abdominal	36	Cerebral	54	Ulnar	39	Carotid, internal	13	Subclavian	88
Aorta, ascending	33	Ulnar	52	Tibial, anterior	37	Aorta, ascending	13	Cerebral	87
Carotid, common	32	Splenic	46	Axillary	36	Subclavian	12	Carotid, internal	87
Femoral, superficial	31	Tibial, anterior	45	Splenic	29	Tibial, anterior	11	Radial	86
Axillary	29	Femoral	44	Carotid, common	28	Popliteal	10	Splenic	82
Carotid, external	22	Popliteal	44	Radial	27	Carotid, common	9	Popliteal	79
Popliteal	21	Aorta, ascending	41	Popliteal	25	Femoral	18	Carotid, external	78
Splenic	18	Brachial	40	Aorta, abdominal	24	Splenic	7	Axillary	71
Radial	14	Iliac, external	38	Iliac, external	19	Carotid, external	6	Femoral	69
Carotid, internal	13	Axillary	34	Cerebral	18	Radial	3	Carotid, common	68
Cerebral	13	Carotid, common	31	Femoral	17	Ulnar	3	Aorta, ascending	67
Subclavian	12	Subclavian	29	Carotid, external	16	Axillary	1	Aorta, abdominal	64
Tibial, anterior	7	Carotid, internal	26	Brachial	15	Iliac, external	1	Iliac, external	58
Ulnar	6	Aorta, abdominal	24	Aorta, ascending	13	Brachial	0	Brachial	55

In this table no distinction is made as regards the kind of arteriosclerosis.

Order of Frequency of Nodular and Diffuse Arteriosclerosis in Different Arteries.

Bregmann

Nodular Form.	*Diffuse Form (in Thoma's Sense).*
Abdominal aorta.	Radial.
Common carotid.	Ulnar.
Descending thoracic aorta.	Anterior tibial.
Internal carotid.	Popliteal.
Ascending aorta.	Splenic.
Arch of the aorta.	Superficial femoral.
Cerebral.	Axillary.
Subclavian.	External iliac.
Common iliac.	Brachial.
Celiac.	Subclavian.
Superior mesenteric.	External carotid.
Inferior mesenteric.	Cerebral.
Renal.	Internal carotid.
Coronary.	Ascending aorta.
Popliteal.	Common carotid.
External carotid.	Abdominal aorta.
Splenic.	
Axillary.	
Common femoral.	
External iliac.	
Posterior tibial.	
Superficial femoral.	
Deep femoral.	
Internal iliac.	
Brachial.	
Anterior tibial (below).	
Ulnar.	
Anterior tibial (above).	
Radial.	

much more advanced in some arteries than in others—those of the brain may be stiff and hard or the coronaries may be extensively changed, while those in other regions may be smooth.

Arteriosclerosis of the pulmonary artery is exceedingly rare as compared with the frequency of the process in the aorta. In chronic tuberculosis of the lungs, emphysema and other diseases resulting in atrophy and destruction of lung tissue give rise to more or less endarteritis. In Saunè's thesis are collected twelve cases of sclerosis of the pulmonary artery; in seven, emphysema was present. It is suggested by Laache that the carbonic dioxide may tend to prevent the development of arteriosclerosis, although the mode of action is not clear; probably the more important factor is the low pressure in the pulmonary artery as compared with that of the aorta (Laache, Saunè).

Laache has described an instance of sclerosis with atheroma of the pulmonary artery that clinically presented the symptoms of congenital heart disease ("morbus cœruleus"); there were hypertrophy of the right ventricle, marked nodular condition of the intima, and dilatation of the pulmonary artery.

Huchard and von Schrötter describe each a case of sclerosis in the pulmonary artery associated with pressure upon it by an aortic aneurysm.

Consequences of Arteriosclerosis.—In consequence of the loss of resistance and elasticity in sclerotic arteries dilatations may take place and aneurysms may develop, especially in the aorta; smaller arteries (splenic, coronary, temporal) become convoluted and also dilated. The dilatation of the aorta and its branches may lead to hypertrophy of the left ventricle. Sclerotic changes in the beginning of the aorta may lead to a relative insufficiency of the aortic valves or by extension to organic stenosis and insufficiency with their consequences; the orifices of the coronary arteries may also become involved. In smaller vessels sclerosis causes narrowing and occlusion often associated with thrombosis so that the nutrition of the organs supplied is interfered with.

Phlebosclerosis.—The early observations on sclerosis of the veins were made by Hodgson, Rokitansky, Virchow, and others. Lobstein introduced the term phlebosclerosis. Rokitansky described thickening of the intima and of the adventitia of the veins involved in varicose aneurysm; and Virchow called attention to chronic endophlebitis in long-continued passive congestions; in both cases the influence of mechanical causes is quite evident.

According to the studies of Sack the localization of phlebosclerosis is determined largely by the same factors as that of arteriosclerosis, and the tendency has been to regard phlebosclerosis as due to general nutritional disturbances resulting in weakness of the middle coat. But it may appear as a local disease in consequence of local venous congestions, as, for instance, in the portal system in atrophic cirrhosis of the liver, and in the pulmonary veins in mitral stenosis. As will be seen from the adjoining table, phlebosclerosis attacks especially those vascular provinces in which the venous pressure varies greatly in different positions of the body, and in which the activity of the voluntary muscles favors the venous flow to relatively but a slight extent. Now every obstruction to the venous flow hinders also the arterial flow, though in a much smaller degree, and possibly phlebosclerosis in some cases precedes arteriosclerosis. Sack showed by the statistical method that the two diseases are closely related. There is need of further study of these questions.

Sack's Table Showing the Distribution of Phlebosclerosis.

	Number of bodies examined.	Number with phlebosclerosis.	Frequency of disease in percentages.
V. jugularis interna.	70	7	35
V. brachialis.	55	4	7
V. cephalica	6	3	50
V. basilaris.	7	4	57
V. radialis	52	0	0
V. ulnaris.	58	0	0
V. iliaca externa	64	23	38
V. femoralis	67	51	76
V. poplitealis	72	65	90
V. saphena magna	55	50	91
V. saphena parva	14	13	93
V. tibialis anterior	88	24	27

Sclerotic veins are elongated and of varying caliber. They present constrictions and dilatations, the dilatations amounting in some cases to well-marked pouches filled and distended with blood. In the severer forms of the disease the vessels are curved upon themselves, and if superficial, they can be rolled under the finger like a cord.

The valves are insufficient, either from retraction of their leaflets or from adherence to the side of the vein. When the vein is cut open its walls show differences in thickness, at one point being strong enough, perhaps, to gape open like an artery, at another collapsing as a vein usually does. At times, portions of the veins show calcified plates and ulcerous spots, resembling in each case those so frequently found in arteriosclerosis. The most marked changes take place in the intima and the inner part of the media. The coats are thickened and present points of fatty changes and of necrosis often infiltrated with lime salts; at other points atheromatous débris may have formed.

Syphilis.—Some of the earliest observations on syphilis of the blood-vessels, as it affects the arteries at the base of the brain, were made by Virchow and Lancereaux. A good anatomical description of syphilitic arteritis was given by Allbutt in 1868. In 1874 Heubner published a study of fifty cases of syphilis of the cerebral vessels, in which he endeavored to establish a primary endothelial proliferation

("arterioma") as the specific form of arterial syphilis, the virus acting directly on the intima. In this he was opposed by Baumgarten, who, while not denying that syphilis causes endarteritis, yet claimed that the only arteritis anatomically characteristic of syphilis begins in the lymph spaces of the adventitia and results in a gummatous periarteritis. Köster, and others support Baumgarten's view, and Friedländer regarded Heubner's endarterial proliferation as indistinguishable from endarteritis obliterans in general. According to this view the virus, *i.e.* the *Treponema pallidum*, acts principally upon the adventitia through the vasa vasorum and the lymph vessels, the inflammatory process extending inward.

Syphilis of the Smaller Vessels.—At the present time the general teaching is that syphilis of the smaller vessels occurs either as an independent process or as part and parcel of a local syphilitic infiltration. In the primary form the vessels involved usually present yellowish-white or grayish thickening of the adventitia and the intima. A smaller vessel, such as a cerebral artery for example, may be

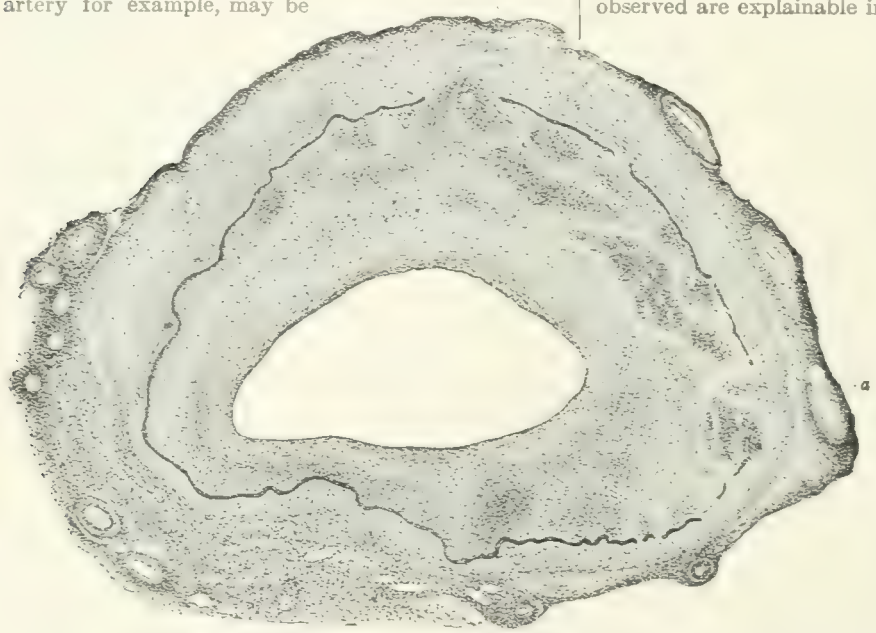

FIG. 832.—Gummous Arteritis. Great intimal thickening with small cellular areas—gummata. At *a*, perivascular infiltration of intima. (From Nothnagel's "Specielle Pathologie und Therapie," xv., p. 147.)

studded with translucent or whitish, circumscribed patches, more or less cartilaginous in consistency and non-calcified; or a certain length of the vessel may be transformed into a whitish cord. The tendency to fibrous obliteration of the lumen is pronounced, but in the earlier stages the proliferation in the intima is richly cellular and vascular. The occurrence of obliterating endarteritis in circumscribed form in youthful persons is regarded, as in the majority of cases, the result of syphilis. It is unquestionably syphilitic when associated with gummous nodules. The new tissue in the intima may contain vascular spaces. The elastic layer is greatly thickened and folded and bands of elastic fibers appear in the thickening. The elastic elements do not appear to differ in their behavior from that seen in endarteritis obliterans in general.

At other times the vessels are surrounded either with nodular, cellular infiltrations or dense cicatricial tissue. In the primary syphilitic lesion there is marked periarterial infiltration, which is surrounded by an external ring of elastic elements, probably part of the walls of the perivascular lymph spaces in which the cellular proliferation takes place. In later syphilitic foci, when the granulation-tissue formation is in the recent stage, there is cellular infiltration in the adventitia, media, and intima. Distinct gummous nodules, either purely cellular (lymphoid and epithelioid cells) or with a granular, necrotic center and a cellulofibrous periphery with giant cells, may be found in the vessel wall (Baumgarten's gummous arteritis), most frequently in the adventitia. This is the only form of syphilitic arteritis that is anatomically specific (Fig. 832).

The gummata develop especially in the adventitia, more rarely in the media and the intima. Occasionally a single cross-section may show a series of nodules in the various layers of the wall. Later, when fibrous transformation takes place, all the coats become fibroid, the media atrophic.

Gummous periarteritis and productive endarteritis are often more or less intimately associated, especially when they occur as consecutive processes in the midst of syphilitic foci. The different appearances so often observed are explainable in a measure by the degree and the duration of the disease. Syphilitic arteritis differs from arteriosclerosis by its circumscribed occurrence and by the tendency to organization and obliteration; fatty changes and calcification are not characteristic of syphilis.

Most of the investigations on syphilis of the smaller arteries concern the cerebral. The apparent frequency with which the cerebral vessels, especially at the base, are affected by these processes is explained as in part the outcome of the great interest that clinicians take in all the phases of cerebral syphilis, and perhaps also because the basal vessels are constantly bathed in cerebrospinal lymph. The anterior cerebral arteries —the cerebral branches of the internal carotid— are the ones especially involved. But syphilitic vasculitis as an independent process occurs elsewhere. In the spinal cord both arteries and veins may be involved. The coronary arteries, the arteries of the extremities, the splenic, the retinal, the mesenteric, and the adrenal may be diseased more or less extensively as well. Syphilitic changes in the coronary arteries may be primary or consecutive, the left coronary artery being affected more frequently than the right.

Haga and others describe syphilitic arteritis of the extremities. In Haga's case the vascular disease resulted in spontaneous gangrene; this form of spontaneous gangrene seems comparatively frequent in Japan. Haga reports thirteen cases, in all of which the vessels of the affected extremities presented the same changes. The vascular lumen was obliterated either as the result of successive intimal thickenings, due to the production of a vascular new tissue solely, or from thrombosis. The media was thickened. In nine of the thirteen cases there were focal accumulations of round cells about the vasa vasorum, and in some instances cellular nodules were present in the media and the

intima (gummous arteritis). Quite similar changes were observed in the veins.

Syphilis of the Aorta and Larger Vessels.—Isolated instances of large gummas, in the walls of the larger arteries, especially the pulmonary, have been described by Weber, Wagner, Virchow, and others. Weber describes a gumma as large as a bean in the pulmonary artery, beginning in the media under the intact intima and causing great narrowing of the lumen.

Wagner and others described a primary syphilitic mesaortitis which Heiberg was the first to interpret as syphilitic in its nature because he found in the lesions miliary gummas. The intima may present circumscribed, fissured and furrowed areas and depressions which occur in groups, especially at the beginning of the aorta and near the origin of the larger vessels. Elsewhere the intima may be smooth and normal or the seat of ordinary sclerotic changes. Bollinger has described a gummous form of endarteritis, and irregular aortic ulcerations with callous margins have been regarded also as of syphilitic origin. In the circumscribed areas of fibrous attenuation of the aortic wall, the media may be necrotic and degenerated, almost wholly absent, or replaced by a thin layer of scar tissue. Microscopically there is proliferation about the vasa vasorum which may show obliterative changes and there may be more or less distinct gummas with necrotic centers as well as cicatricial areas with thickening of the intima and retractions giving the peculiar linear and circular pit-like depressions that are regarded as characteristic of syphilitic mesaortitis. Foci of small round-celled infiltration as well as diffuse fibrous changes occur in the intima. Benda holds that the more advanced changes always represent terminal stages of aortic gummas. Wright and Richardson and others have demonstrated the presence of the spirochetes in the more cellular and necrotic lesions just outlined. Of other facts pointing to the syphilitic nature of these lesions may be mentioned that Chiari found such lesions in one-half of the syphilitics and paretics which he had occasion to examine after death and Straub found them in eighty-two per cent. of the paretics that he examined; furthermore, that there are often, as would be expected, distinctly syphilitic lesions in other organs. The changes are observed not rarely in rather young persons and it is on the basis of such changes that aneurysms in syphilitics often develop. It may be recalled that the percentage of syphilis in patients with aortic aneurysms greatly exceeds that of syphilis in the general population. Syphilis is also regarded as playing an etiological rôle of a more general nature or of greater importance in the ordinary form of arteriosclerosis, but on account of the many complicating factors concerned, the exact rôle of syphilis in the causation of arteriosclerosis is hard to define.

Syphilitic Phlebitis.—Much that has been said of syphilis of the arteries is applicable to syphilis of the veins especially as regards the secondary changes that occur in smaller veins in the midst of larger syphilitic foci.

Oedmanson and others have described diffuse and circumscribed endophlebitis of the umbilical veins of congenital syphilitics. Schüppel has described a gummous pylephlebitis in congenital syphilis, and Bowman attributes certain cases of thrombosis of the stem of the portal vein to syphilitic periphlebitic changes. Huber found intimal thickening with petrifaction in the veins of the extremities of a syphilitic girl twenty-two years old.

The vascular changes of the lesions of *congenital syphilis* in the internal organs resemble those of the acquired disease. Diffuse and localized arterial lesions may occur, sometimes early, sometimes as a late manifestation in *syphilis hereditaria tarda* (Osler). Virchow observed an ossifying endaortic process in a girl of eighteen with congenital syphilis. Reference has been made to Scriba's view that spontaneous gangrene may be caused by an arteritis of congenitally syphilitic origin.

Tuberculosis. Older pathologists, such as Rokitansky and Virchow, regarded the blood-vessels as immune to tuberculosis. The demonstration by Weigert in 1877 that acute general miliary tuberculosis results from the tuberculous invasion of either a blood-vessel or the thoracic duct put an end to this view. So thoroughly did Weigert demonstrate this course of events that when the tubercle germ was discovered a few years later he could say truthfully that it was necessary only to substitute bacillus for poison in order to make the report of his investigations conform fully to the new requirements.

Tuberculosis of the walls of blood-vessels may result from the extension of the process from adjacent tuberculous foci. This may occur in the arteries and veins. In case the lumen is not closed by productive endovasculitis and thrombosis, the infiltration in the vessel wall on caseation and disintegration may give off tuberculous material and bacilli to the circulating blood. This leads to embolic or miliary tuberculosis of the corresponding capillary district. In the case of the pulmonary vein, the general circulation becomes infected; in the case of a systemic vein, miliary tuberculosis of the lungs results; and if it concerns an artery, miliary tubercles may spring up in its capillary district. Tuberculous and suppurative destruction from without of the branches of the pulmonary artery exposed in tuberculous pulmonary cavities may so weaken the wall that aneurysmal dilatations develop ("erosion aneurysm"). Many of the copious hemorrhages in advanced pulmonary phthisis result from the rupture of aneurysms of this nature.

Dittrich and others have described tuberculosis of the wall of the aorta due to direct extension. In Dittrich's case an adherent lymph gland communicated the disease to the thoracic aorta, the intima of which presented an oval defect with elevated ridges, a continuous tuberculous process traversing the aortic wall. Kamen's case was of similar origin, the vessel presenting a dilatation with rupture of the wall. In Sigg's case a tuberculous lung was adherent to the aorta, which presented a bulging corresponding to the caseous replacement of its wall, the caseous area being covered internally by a thrombus.

When tubercle bacilli reach the circulating blood they sometimes become implanted upon the intima of larger vessels such as the aorta. Weigert, Flexner, Blumer and others have described pinhead-sized intimal, aortic tuberculous masses. Blumer describes two instances of intimal tuberculosis of the abdominal aorta; in one of the cases there were several minute nodules of characteristic structure. The sclerosis of the aorta present in both cases did not play any part in determining this localization. In all of these cases the infection took place directly upon the intima and not through the vasa vasorum or the lymphatics of the walls of the artery. The tuberculous masses appeared as if they had been fastened upon the intima. The surface of such areas may contain tubercle bacilli in large numbers.

According to Cadéac tuberculous aortitis is not uncommon in cattle. I have studied a tuberculosis of the aorta in a dog. A large nodule developed in the wall of the aorta near the heart, producing such weakening that a small bulging had resulted.

The relation of tuberculosis of the blood-vessels to general miliary tuberculosis is discussed elsewhere. At this time it is sufficient to say that tuberculosis of the intima of blood-vessels or of the thoracic duct or tuberculous endocarditis constitutes an essential, intermediate stage in the development of acute general miliary tuberculosis. It is in the tuberculous areas that result from infection of the intima (and of the endocardium) that the germs multiply so freely that

masses are thrown into the general circulation and produce on lodgment in the internal organs the numberless nodules characteristic of general miliary tuberculosis. There being no satisfactory evidence that tubercle bacilli multiply in the blood miliary tuberculosis means the setting free in the circulation at one time of large numbers of bacilli (Weigert, Benda, Gaylord).

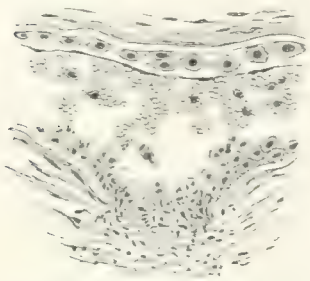

FIG. 833.—Perforation of the Elastic Layer by Caseous Intimal Focus, Infiltration into Media and Adventitia, and Beginning Aneurysmal Bulging. Note beginning subendothelial proliferation in opposite wall from tuberculous leptomeningitis. (Hektoen, *The Journal of Experimental Medicine*, vol. i.)

The vascular changes in tuberculous leptomeningitis are interesting and well marked. There is a tuberculous endarteritis characterized by the formation of intimal tubercles and a diffuse subendothelial intimal proliferation (Figs. 833 and 834), probably induced by the implantation of tubercle bacilli from the blood. From the intima the infiltration may spread into the muscular coat and the adventitia and the whole wall may undergo caseous and hyaline degeneration. Occasionally, though rarely, the intimal process so weakens the wall that small, local dilatations take place—a species of mycotic aneurysm. Proliferation in the adventitia may invade the media and the intima and the whole wall of the arterial segment may undergo degeneration. In tuberculous leptomeningitis the muscularis often presents the hyaline degeneration described by Guarnieri and others. The epithelioid cells that constitute such a prominent feature of the intimal proliferation undoubtedly originate from the subepithelial connective tissue rather than from the epithelial lining, which appears to remain intact until caseation takes place. Plasma cells and phagocytic cells are also present.

In this form of tuberculosis adjacent extravascular and arterial foci frequently extend to the veins (Fig. 835).

Banti describes a case of general tuberculosis in which nearly the whole length of the superior vena cava was completely filled by a mass of neoplastic tuberculous tissue which projected into the right auricle.

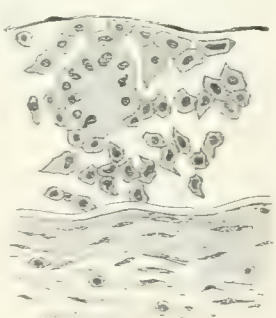

FIG. 834.—Subendothelial Intimal Proliferation with Multinuclear Giant Cell. From tuberculous leptomeningitis. (Hektoen, *The Journal of Experimental Medicine*, vol. i.)

ACTINOMYCOSIS.—As actinomycosis spreads through the tissues by direct extension; no anatomical structure is secure from invasion, not even the blood-vessels. In metastatic actinomycosis the fungus gains entrance into the circulation by the direct involvement of the walls of the blood-vessels in the vicinity of a local process. In the cases in which the point of invasion of the vascular system has been directly demonstrated it concerns some of the larger veins and cerebral sinuses.

The meningeal sinuses and veins are frequently attacked in craniocerebral actinomycosis. In many cases of actinomycotic phlebitis the generalization of the process is undoubtedly prevented or delayed by consecutive thrombosis.

Ponfick describes an actinomycotic proliferation which projected button-like into the lumen of the internal jugular vein; this invasion became the direct or indirect source of secondary foci in the heart, lungs, spleen, and brain.

In a case of primary pulmonary actinomycosis with extension through the diaphragm and into the spleen, Paltauf found the splenic vein infiltrated and thrombosed, the thrombosis extending into the portal vein; there were metastatic foci in the liver and in the brain. Others describe perforation in the hepatic vein in a secondary actinomycosis of the liver. In pulmonary actinomycosis with extension to the pleura and pericardium Habel found the base of the heart and the larger vessels surrounded by a spongy tissue; just above the entrance into the auricle the superior vena cave presented a circumscribed area in which the normal wall was substituted by a nodular mass of pale yellow color; the jugular veins were thrombotic. Actinomycotic perforation of the inferior vena cava has been observed (Abée). Beginning in the esophagus the process spread out in the prevertebral, mediastinal, and peripleural tissue, and invaded the diaphragm and the spinal column. The infiltration between the right lung and the diaphragm surrounded the inferior vena cava in the form of a layer, three to four centimeters thick, of a reddish, soft tissue riddled with confluent abscesses. At the point where the vein entered the auricle its lumen was materially narrowed, the intima roughened, covered by parietal thrombi and perforated by numerous yellowish suppurative foci; below, the vein was partially filled with a large softened thrombus. There were numerous metastatic actinomycotic abscesses in various parts of the body.

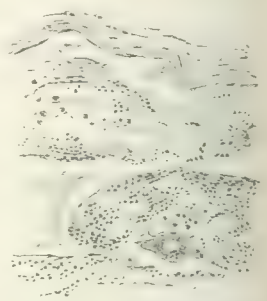

FIG. 835.—Focal Tuberculous Infiltration with Giant Cell, Extending through Wall of Vein with Secondary Thrombosis, Caused by Extension in Tuberculous Leptomeningitis. (Hektoen, *The Journal of Experimental Medicine*, vol. i.)

LEPROSY.—Leprous nodules sometimes occur in the walls of the veins in leprosy of the extremities.

PERIARTERITIS NODOSA.—This remarkable disease was described by Kussmaul and Maier in 1866. Cases had been observed previously by Pelletan in 1810 and by Rokitansky, but their descriptions were confined to the macroscopic appearances. Since Kussmaul and Maier fastened attention upon the disease additional instances have been recorded, so that the total number of cases now is thirty-one (Künne, 1910). The disease appears to attack young persons mostly between twenty and thirty; it occurs also in children. The male sex has so far furnished more cases. The symptoms are, generally speaking, those of a more or less severe polyneuritis and polymyositis with constitutional and digestive disturbances, abdominal pain, renal symptoms, etc. In several cases the diagnosis has been chronic nephritis. In many cases there has been observed a moderate leucocytosis. In nearly all cases anemia and general weakness have been recorded. The whole course of the disease as a rule takes from six to twelve weeks, the termination as far as known being always fatal. In a few cases the patients lived from four months to one or two years. In Kussmaul and Maier's instance minute nodules were present in the skin of the face, neck, and upper extremity. It is quite likely that in the future the

disease will be diagnosed during life, especially in instances with subcutaneous nodules which might be excised and examined microscopically. A correct diagnosis, substantiated by histological examination of nodules, has been made only twice during life, once by Schmorl and once by Benedict. In both cases the diagnosis was made from an examination of an excised subcutaneous nodule (Longcope). In these cases the disease lasted almost two years and its course seemed to be influenced by iodide of potassium. Clinical observation has not brought out any common or striking etiological conditions. Syphilis has been present in some cases and definitely excluded in others. Lüpke has described a disease like periarteritis nodosa in stags.

The vascular lesions consist of nodular, excentric, and more diffuse thickenings of arteries of the general size of the coronaries and hepatic and smaller; the swellings are grayish and grayish-white in color, vary in size from pinhead to pea and larger, occur especially at the branchings, but also in the course of the arteries both when free and intraparenchymatous. The distribution and number of the swellings, usually present in great numbers, vary somewhat in different cases (Weichselbaum and Thompson); the favorite locations are the mesenteric (including the intraparietal branches of the gastrointestinal tract), and the coronary, then the muscular, intraneural, renal, hepatic, splenic, bronchial, and subcutaneous. Cooke observed a case in a Russian, nineteen years old, in Philadelphia, in which there was an acute hemorrhagic and glomerular nephritis and in this case the arterial changes were most marked in the kidneys. Nodules have also been described at the origins of the intercostal branches of the aorta and of branches of the crural and popliteal arteries. It is noteworthy that up to this time the veins have not been involved (Fig. 836).

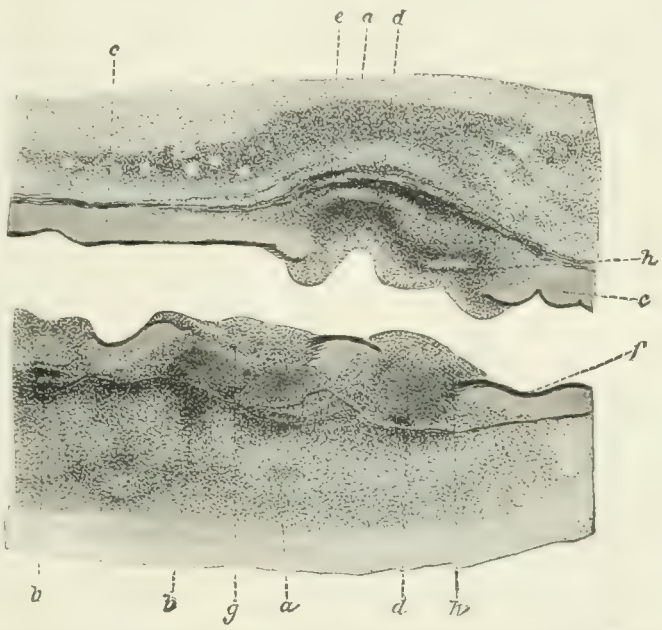

Fig. 836.—Periarteritis Nodosa. Longitudinal section of a small muscular branch. (After Freund.) *a*, Adventitia, greatly infiltrated with cells; *b*, foci of especially dense cell accumulations in adventitia; *c*, normal media; *d*, degenerated media; *e*, external elastic lamina, bulging outward; *f*, internal elastic layer; *g*, remnants of internal elastic layer; *h*, proliferating intima.

The histogenesis of the arterial lesions, which are of an inflammatory nature associated at times with aneurysmal dilatations, fibrous tissue formation and thrombosis, is not agreed upon. Fletcher, von Kahlden, and Freund regard the process as primarily inflammatory, due to the action of some unknown substance, which reaches the vessel by way of the vasa vasorum. This view is supported by the presence, in Fletcher's case, of nodules upon the vasa vasorum and by the microscopic appearances in the early stages of the process (Freund). Accordingly, the inflammatory infiltration, which appears to be of a non-specific type, begins in the adventitia and extends through the media to the intima, producing in the last marked cellular accumulations between it and the media. As a result of the inflammation the muscular coat undergoes a circumscribed hyaline degeneration, and hyaline material, probably of exudative origin, also appears in the subepithelial layers. (Künne regards the changes in the media as primary.) There are not many polymorphonuclear cells in the cellular infiltration, which consists largely of spindle-shaped cells with large nuclei. Freund did not find proliferation in the intima when the media was normal. Eventually the internal elastic coat and the media are so thinned and destroyed that circumscribed aneurysmal bulgings of the vessel wall may occur, but the formation of aneurysms is not constant because the development of fibrous tissue may prevent dilatation. Longcope holds that perivascular accumulations of small round cells conconstitute the earliest stages of the process.

Others, like Weichselbaum and Chvostek, hold that the process is primarily an endarteritis, which extends to the outer coats. In the case of smaller arteries and of vasa vasorum this would seem to be the fact probably. Others again believe that the process begins in the media with edema and degenerations (Benda, Ferarri, *et al.*).

It has been suggested that periarteritis nodosa is a primarily multiple tumor of the nature of lymphoma, beginning in the adventitia. Circumscribed accumulations of cells occur in the adventitia that resemble lymphomata; but the singular fact that the process is confined to arteries speaks against this view. The subsequent formation of fibrous tissue is also inconsistent with this theory.

Meyer regarded tears in the media as the essential cause, and Eppinger has elaborated the theory that periarteritis nodosa is the result of the formation of multiple aneurysms on account of ruptures of the elastic elements, which are congenitally weak and imperfect. Eppinger proposes to call the disease congenital aneurysm. The proliferation observed in the adventitia and intima, which constitutes such a striking feature of the lesions, is regarded by him and the supporters of the aneurysmal theory as secondary; and the thrombi and hard fibrous masses sometimes observed are similarly explained. Aneurysms are not observed in every instance of periarteritis nodosa; in some cases they are marked. In Pelletan's case sixty-three aneurysms were present. The development of aneurysms is consistently explained on the score of more marked inflammatory and degenerative weakening of the arterial wall in some nodules than in others in which these processes were not so rapid. Any evidence of anatomical nature of a congenital structural imperfection of the arteries in periarteritis nodosa has not been furnished. Eppinger's theory does not satisfactorily explain the relative infrequency of involvement of the cerebral arteries, which would seem to be as liable to aneurysmal dilatations as other arteries, if not

more so. The clinical course of the disease is also against this view.

The appearances and the genesis of the changes as explained by Freund and others favor the view that periarteritis nodosa is a primarily inflammatory process in the further course of which aneurysms frequently develop; but further studies are essential before the question of the nature of this disease can be definitely established. Microorganisms have not been found in the lesions. Syphilis has been suggested as the underlying condition. The absence, in some cases of periarteritis nodosa, of all history of syphilis and the freedom of other organs from syphilitic lesions and their consequences are also against the specific theory; and it does not appear that the vascular lesions of periarteritis nodosa ever present nodular foci of cell accumulations with central necrosis such as occur in the gummous form of syphilitic arteritis. All attempts to demonstrate *Treponema pallidum* in the nodules have failed. The fever, the leucocytosis, the inflammatory nature of the changes, and the renal lesions all point to an infectious origin.

Many of the clinical symptoms are evidently due to secondary lesions in the internal organs. Although the intramyocardial branches of the coronary arteries are generally involved, the myocardium itself usually presents but slight changes. Whether bronchitis and other inflammatory changes in the lungs are directly secondary to changes in the bronchial arteries, the pulmonary being usually free (von Schrötter), cannot be stated. The mucous membrane of the gastrointestinal tract has been found to be the seat of multiple ulcers and hemorrhages; the ulcers in the stomach being more of the nature of erosions while those in the intestines may resemble typhoid ulcers. These changes are regarded as the result of circulatory disturbances in the areas nourished by the affected branches, many of which become entirely occluded by thrombosis. Enlargement of the mesenteric glands is usually present. The spleen may be the seat of infarcts, in various stages of absorption, caused again by the occlusion of terminal arteries. Pressure of the nodules in the intrahepatic branches of the hepatic artery on the bile ducts may cause jaundice. Severe changes are produced in the kidneys. Multiple ischemic necrosis results from thrombosis of the affected arteries. Degeneration of the glomeruli, glomerulitis, hemorrhages, parenchymatous and interstitial changes develop, due either to extension of the vascular changes or to the action of toxic substances in the blood. The changes in the peripheral nerves and in the skeletal muscles explain well the nervous and muscular phenomena observed clinically. The pressure of changed arteries upon adjacent nerves may cause degenerations, and in Freund's case foci of degeneration in the nerves were found to correspond to nodules upon intraneural arterial branches. The development of nodules upon the intramuscular arteries gives rise to granular and fatty disintegration of the muscle fibers and to waxy changes.

In Weichselbaum's case the rupture of an aneurysm, two centimeters in diameter (the largest so far recorded in periarteritis nodosa), upon the arteria profunda cerebri gave rise to hemorrhage.

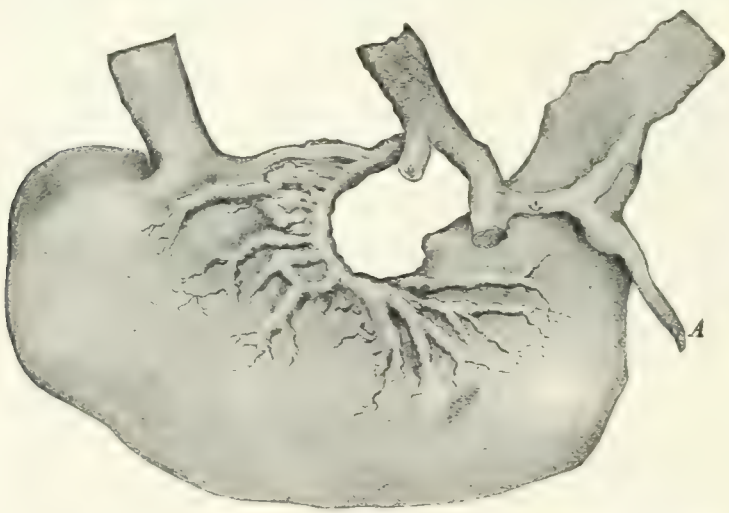

FIG. 837. Growth of Carcinoma into the Gastric and Portal Veins and the Radicles of the Latter, Secondary to Carcinoma of the Pylorus. The posterior surface of the stomach, which is turned so that the pylorus is to the left, is exposed. *A*, Cut end of gastroduodenal vein.

TUMORS.—The primary tumors composed of blood-vessels—the various forms of angioma—are described in the article on *Tumors*. Here is described also the part that blood-vessels play in the general dissemination of the malignant tumors. Primary tumors rarely develop in the walls of blood-vessels. Brodowski has described a primary sarcoma of the thoracic aorta, which started in the adventitia and extended through the muscular coat and into the intima; the sarcomatous infiltration of the intima produced a marked thickening of the latter.

I have described an interesting pedunculated outgrowth of the intima of the basilar artery, which at that time was regarded as a fibroma. It is possible, however, that the outgrowth in reality was the result of an endarteritic proliferation of inflammatory nature.

Several instances of myoma, fibroma, and sarcoma have been described as primary in veins (Orth).

Secondary tumors occasionally occur in the walls of the blood-vessels. Broca described a cancer at the root of the aorta with rupture into the pericardium, Friedrich, metastatic nodules of a papillary cystocarcinoma of the ovary in the wall of the thoracic and abdominal aorta and the renal artery; here the metastases evidently occurred through the vasa vasorum. The nodule in the thoracic aorta ruptured into the lumen of the vessel.

Extensive intravascular growth of malignant tumors, especially in the veins, takes place in the case of sarcoma of various kinds, notably of the bones, in adrenal tumors of the kidneys, etc. Intravascular growth of this kind has extended from the renal vein, for instance, to the heart.

In carcinoma of the stomach I have observed an extensive intravenous growth of the tumor resulting in a kind of carcinomatous injection of all the veins about the lesser curvature of the stomach and of the portal vein (Fig. 837). Orth observed the entire venous plexus of the dorsum of the foot filled with sarcomatous masses.

Norïca and Haret describe a carcinoma of the stomach with metastases in the mesenteric, mediastinal, and deep cervical glands, followed by carcinomatous invasion and thrombosis of the superior vena cava, the two brachiocephalic, subclavian, and internal jugular veins. There was dilatation of the subcutaneous veins on the right side. In 1885 Oulmont collected nineteen cases of obliteration of the superior vena cava. He distinguished two groups, namely, obliteration by pressure and obliteration by concretion. The first group comprised five cases due to cancer of the mediastinum or of the lung, two cases

due to tuberculous lymph glands, and four cases due to aortic aneurysm. The second group included five cases of thrombosis and three cases of cancerous invasion. Comby and Rendu each report a clinical case in which aneurysm of the aorta was thought to be the cause. I have examined post mortem a case in which an aneurysm of the ascending aorta compressed the superior vena cava, which was wholly obliterated by the formation of fibrous tissue in the intima. The occlusion took place gradually and resulted in a great dilatation of the subcutaneous thoracic and abdominal veins which for years furnished routes for collateral circulation. Letulle lays stress on occlusion of the large veins of the neck and mediastinum on account of propagation of carcinomata of the glands, the thyroid, and the thymus.

LUDVIG HEKTOEN.

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Blood-vessels, Plastic Surgery of.—See *Arteries, Surgery of.*

Blount Springs.—Blount County, Alabama.

POST-OFFICE.—Blount Springs. Hotel.

ACCESS.—On the Louisville and Nashville Railroad, thirty-five miles north of Birmingham.

The waters of Blount Springs may be classed as saline sulphureted. The principal springs are six in number, Red Sulphur, White Sulphur, Sweet Sulphur, Arsenic-lithia, Hepatic, and Freestone, and are located in a triangular valley 1,580 feet above the sea level.

ONE UNITED STATES GALLON CONTAINS

Solids.	No. 1 Red Spring.	Sweet Spring. Brantley	Spring No. 4. Summers.
	Grains.	Grains.	Grains.
Magnesium carbonate	3.67	3.60	9.40
Calcium carbonate	7.23	1.48	5.72
Barium carbonate			.91
Iron carbonate		1.12	3.19
Sodium carbonate			
Magnesium sulphate	....	2.40	
Calcium sulphate	0.28		1.27
Sodium sulphate	0.89		
Calcium phosphate			Trace.
Potassium chloride			7.07
Sodium chloride	29.86	30.88	23.21
Magnesium chloride	0.78		2.04
Iodides	Trace.		
Magnesium iodide			.14
Magnesium bromide			.16
Lithium			Trace.
Alumina, Silica	3.00		Trace. 2.44
Sulphur	2.01		
Total	47.72	42.48	55.55
Gases.	Cu. in.	Cu. in.	Cu. in.
Carbonic acid	6.00	6.00	4.72
Sulphureted hydrogen	14.96	12.56	30.67
Oxygen			7.08
Nitrogen			

Sulphur in the Red Spring is equal to about five cubic inches to the gallon. The water is recommended for diseases of the stomach, liver and kidneys, and is a powerful alterative tonic. EMMA E. WALKER.

Blow Fly.—Flies of the genus *Calliphora*, family *Muscidæ*, also known as "blue-bottles." They commonly enter dwellings. The larvæ live on carrion or decaying excrementitious matters. See *Insects, poisonus.* A. S. P.

Blue Babies.—See *Cyanosis.*

Blue Hill Mineral Spring.—Hancock County, Maine.

POST-OFFICE.—Blue Hill. Hotels.

ACCESS.—Viâ steamer from Portland, also by stage from Ellsworth, fourteen miles distant.

The Blue Hill Mineral Spring is located two and one-half miles northwest of Blue Hill village, and about 600 feet in perpendicular height above the base of Blue Hill Mountain. Its situation assures freedom from all surface impurities. The existence of the spring was noticed by Dr. Charles T. Jackson in his second report of the geology of the State of Maine, published in 1838. It was not until recently, however, that improvements were made. A handsome and commodious building has been erected for the comfort of tourists and visitors at the springs, and a large bottling plant established.

The following is an analysis of the water by Prof. William P. Mason, of the Rensselaer Polytechnic Institute of Troy, N.Y.:

Potassium chloride	0.99
Sodium chloride	5.00
Sodium nitrate	0.91
Sodium sulphate	5.33
Calcium sulphate	5.61
Manganese carbonate	0.45
Iron carbonate	6.62
Silica	20.56
Alumina	1.89
Magnesium carbonate	6.09
Calcium carbonate	25.16
	78.61

Taste	None.
Odor	None.
Sediment	None.
Turbidity	None.
Chlorine in chlorides	3.05
Nitrogen in nitrates	0.15
Nitrogen in nitrites	None.
"Required oxygen"	1.75
Free ammonia	0.067
Albuminoid ammonia	0.05
Bacteria per cubic centimeter	11.
Bacillus coli communis	None.
Gas-forming bacteria	Absent.

This is an excellent table water, and it also possesses mild diuretic and tonic properties. It is said to be of value in disorders of the kidney and bladder. The water is used commercially. EMMA E. WALKER.

Blue Lick Springs.—Nicholas County, Kentucky.

POST-OFFICE.—Blue Lick Springs.

These springs are located ten miles from Carlisle, Kentucky, on the Louisville and Nashville Railroad. They are also situated on the Maysville and Lexington State Turnpike. The village is on the Licking River, forty-eight miles northeast of Lexington, and is a watering-place.

The following analysis was made in 1905 by the United States Department of Agriculture, Bureau of Chemistry, Washington, D. C.:

	Parts in 1,000
Ammonium chloride	.0022
Lithium chloride	.0109
Potassium chloride	.1331
Sodium chloride	6.9040
Magnesium chloride	.7090
Calcium chloride	.1827
Potassium bromide	.0342
Potassium iodide	.0017
Calcium sulphate	.4822
Sodium nitrate	.0030
Calcium bicarbonate	.5468
Ferric oxide and alumina	.0014
Mangano-manganic oxide	.0181
	9.0234

Blue Lick is a natural aperient water. The water is beneficial in affections of the liver and kidneys, and in dyspepsia, chronic constipation, rheumatism, gout, and cutaneous diseases. EMMA E. WALKER.

Blue Lick Springs.—Saline County, Missouri.

POST-OFFICE.—Marshall. Cottages at spring.

ACCESS.—Viâ Chicago and Alton road to Marshall, thence eight miles by stage south to springs.

Saline County, Missouri, is entitled to eminent distinction as a water-producing district. Thousands of clear, pure-water springs of more or less volume are well distributed over its surface. They are found in large numbers along the Missouri, Blackwater, and Salt River bluffs, and at the base of the minor hills in all parts of the country, and are unfailing at all periods of the year. The most remarkable natural resources of the county, however, are its mineral waters, which for volume, variety, and medicinal value are among the finest in the country. Not less than 2,000 mineral springs, some of them of immense flow, are found in the limits of the county. Some of these springs will, no doubt, take a prominent place among the health resorts of the country when they shall have been properly developed. At the Blue Lick Springs are more than thirty distinct fountains in a pretty valley at the base of picturesque wooded bluffs. The largest of the group, known as the "Gum" Spring, is an immense salt fountain of 57° F., which was formerly the site of extensive salt works, but is now the center of a large bathing establishment. Nearby is the "Blue Lick" Spring, the most important of the group. Then there are numerous black sulphur, magnesian, chalybeate, and sweet springs, besides uncounted saline springs. Many of these have been analyzed by State Chemist Paul Schweitzer:

Lithium has been found in White Sulphur Spring, Sweet Spring, Magnesia Spring, Salt Spring, and Red Sulphur Spring.

It will be seen that the waters are very similar to those of the Blue Lick Springs of Kentucky, for which these springs are named.

The water is well adapted for the treatment of constipation, especially when due to engorgement of the portal system. On the other hand, it is also said to act beneficially in many cases of chronic diarrhea. It acts with advantage in many of the conditions due to a sluggish liver, such as hemorrhoids and jaundice. Being a very efficient diuretic, the water is useful in certain renal and bladder disorders. It is useful also in disorders of the stomach, and in rheumatism. Within sixty steps of the Blue Lick Spring are three black sulphur springs; 250 yards south is the Sweet Spring, which has been found to be a very efficient diaphoretic and diuretic. It is entirely free from sulphur and forms a very pleasant beverage. EMMA E. WALKER.

ONE UNITED STATES GALLON CONTAINS:

Solids	Blue Lick Spring.	Baden Spring.	White Sulphur Spring.	Sweet Spring.	Rock Haven Spring.	Magnesia Spring.	Black Sulphur Spring.	Gum Spring.	Salt Spring.	Red Sulphur Spring.
	Grains	Grains	Grains	Grains	Grains	Grains	Grains	Grains	Grains	Grains
Silica	8.16	3.50	3.74	2.69	0.57	2.69	0.54	0.41	0.88	3.62
Alumina	10.23	.	.	.	0.10	1.60	0.06	.	.	4.74
Ferric oxide	.	.	0.04	.	.	.	.	.	.	.
Calcium carbonate	57.84	37.02	41.75	56.22	29.10	57.02	73.63	44.30	64.99	42.32
Calcium sulphate	.	.	.	.	39.33	51.49	88.28	112.51	113.00	107.05
Calcium chloride	.	.	.	.	32.54	24.55	44.56	102.31	85.89	57.82
Magnesium bicarbonate	.	.	2.29	4.16	.	.	.	.	.	.
Magnesium sulphate	26.13	4.61	12.53	17.60	.	.	.	.	.	.
Magnesium chloride	10.94	.	6.70	5.88	46.08	55.75	89.52	113.27	116.17	148.37
Potassium chloride	.64	.	2.48	1.86	.	21.76	.	.	11.80	14.51
Sodium chloride	493.88	30.96	175.93	212.43	410.89	555.52	945.49	1280.59	1289.17	1292.11
Sodium sulphate	2.48	0.30	.	.	.	.	.	.	.	.
Organic matter	.	.	.	.	.	.	.	.	.	.
Total	610.30	76.39	245.46	300.84	558.61	770.38	1242.08	1653.39	1681.90	1670.54
Temperature of air, 48.3° of springs	.	54.2° F.	54.5° F.	54.4° F.	56.3° F.	54.5° F.	58.9° F.	61.7° F.	62.6° F.	62.6° F.
Gases.	Cu. in.									
Free carbonic acid	53.22									
Sulphureted hydrogen	Not estimated.	Absent.	Trace.	Absent.	Present.	Absent.	Present.	Present.	Present.	Present

Blue Ridge Springs.—Botetourt County, Virginia. POST-OFFICE.—Blue Ridge Springs. Hotel and cottages.

ACCESS.—Viâ Norfolk and Western Railroad. The hotel is located near the railroad station.

This resort has a picturesque location in the midst of the Blue Ridge Mountains, the elevation being about 1,300 feet above the sea level. The springs yield about 120 gallons of water per hour, having a temperature of 52° F. the year round. The water has been analyzed by Prof. Henry Froehling, with the following results:

ONE UNITED STATES GALLON CONTAINS:

Solids.	Grains.
Magnesium sulphate	47.01
Calcium sulphate	100.13
Sodium sulphate	.37
Potassium sulphate	.65
Magnesium carbonate	1.61
Calcium carbonate	3.96
Strontium carbonate	.29
Barium carbonate	.02
Manganese carbonate	.02
Nickel and cobalt carbonate	Trace.
Iron (ferrous) carbonate	.11
Lead carbonate	Trace.
Copper carbonate	Trace.
Sodium chloride	1.26
Lithium chloride	.04
Sodium arsenate	Trace.
Sodium iodide	Trace.
Sodium bromide	Trace.
Calcium fluoride	Trace.
Magnesium nitrate	.35
Ammonium nitrate	.03
Aluminum phosphate	.02
Aluminum silicate	.15
Silicic acid	1.35
Total	157.37
Carbonic acid combined	2.57
Gases.	Cu. in.
Carbonic acid free	38.20
Sulphureted hydrogen	3.00

The water is used commercially. It is pleasant to drink and bears transportation well. It is useful in dyspepsia, especially when attended by acidity, and it seems to act as a corrigent or regulator of secretion, being efficacious both in diarrhea and in constipation. It is used in disorders of the kidneys and in rheumatism. The water also possesses excellent tonic properties. EMMA E. WALKER.

Blumenbach, Johann Friedrich.—Born at Gotha, Germany, May 11, 1752. He received his degree of Doctor of Medicine from the University of Goettingen in 1775, and was appointed, first, Professor Extraordinary of Medicine in 1776, and then Professor in Ordinary in 1778. He died at Goettingen, January 22, 1840.

FIG. 838.—Johann Friedrich Blumenbach.

Blumenbach is known to posterity chiefly as an anthropologist. His earlier published writings treated of topics relating to physiology and comparative anatomy, and they passed through many editions; but his great work on anthropology—of which science he has been justly called the founder—bears the title "Collectionis suæ craniorum diversarum gentium illustratæ decades" (Goettingen, 1790–1828) and contains the description of sixty human crania. He divided the human race into five varieties or families: the Caucasian or white race, the Mongolian or yellow, the Malayan or brown race, the Negro or black race, and the American or red race; and this classification is the one which is still generally accepted. A. H. B.

BNA.—See *Anatomical Nomenclature, the Basle.*

Bobbs, John Stough.—Born at Greenvillage, Pennsylvania, on December 28, 1809. He received the degree of Doctor of Medicine from Jefferson Medical College, Philadelphia, in 1836, and began active practice in Indianapolis, Indiana. According to Stone, from whose "Biography of Eminent American Physicans and Surgeons" the present account has been compiled, Dr. Bobbs had already in 1850 attained the position of Professor of Surgery in the Indiana Central Medical College, and Dean of the Faculty. The following report of the professional qualifications of Prof. Bobbs is from the pen of the late Hon. J. W. Gordon, one of his former students and a personal friend: "His descriptions of healthy and diseased action and the changes from the one to the other, have never been surpassed in point of clearness, accuracy, and graphic force. . . . . The student who did not carry away in his memory such a portrait of each disease described by the professor as would enable him to detect the original when presented for examination, must have lacked some mental endowment essential for success in his profession. Nor was he less remarkable for self-possession, steadiness, rapidity, and accuracy in the use of the knife. . . . . He always held his profession sacred, high above all trickery and quackery, and labored with incessant diligence to place it in public estimation upon the same footing it held in his own regard. . . . . To the poor and needy he was always wisely kind and beneficent. When called upon professionally to attend the sick of this class, he was known in innumerable instances to furnish, besides gratuitous service and necessary medicine, the means of life during their illness." Dr. Bobbs, it appears, was the first surgeon in this country to perform the operation of cholecystotomy. Dr. Kemper,* who gives a detailed account of the operation, speaks of Dr. Bobbs' achievement in the following terms: "When the operation of cholecystotomy shall have been placed on a firm and scientific basis, and recognized and acknowledged by our profession—as assuredly it will—and its literature fully considered, the luster of no name on its roll shall exceed that of Dr. Bobbs."

Dr. Bobbs died at Indianapolis on May 1, 1870. A. H. B.

Bocconia.—A powerfully medicinal and poisonous genus of plants in the *Papaveraceæ* or Poppy family. "*B. cordata* Willd.," more properly *Maclaya cordata* (Willd.) R. Br., of China and Japan, is a stout perennial herb, largely cultivated as an ornamental plant, the roots of which are used medicinally. It contains at least three alkaloids (*vide* Schlotterbeck), namely, protopine in large amount, β-homochelidonine, and chelerythrine, and possibly sanguinarine also. *B. arborea* Watson, of Mexico, and *B. frutescens* L. and *B. integrifolia* Kunth. of tropical America, are small trees or large shrubs, the bark of which is used similarly. These barks are rich in alkaloids and resinous matter. The alkaloids have been isolated and somewhat studied in the Instituto Medico Nacional of Mexico, and names assigned them; but apparently insufficient care was taken in comparing them with known alkaloids of other members of the

* Transactions of the Indiana State Medical Society for 1868. See also vol. ii. page 118, of the first edition of this HANDBOOK.

family, notably of sanguinaria. If they are not absolutely identical with the latter, they are at least very similar in physiological action, as well as chemically. These drugs have been very little studied in any way, but richly deserve it. The writer has found the leaves of *B. frutescens* highly prized among the Indians of South America, but their uses there give little clue to their special properties. H. H. Rusby.

Bodo.—*Cystomonas.* A genus of parasitic *Protozoa*, family *Bodidæ*, class *Mastigophora*. These flagellates have no undulating membrane and one of the flagella is usually bent backward and kept close to the body. One species, *B. urinaria*, has been observed in human urine. See *Protozoa*. A. S. P.

Boerhaave, Hermann.—Born Dec. 31, 1668, in Voorhout, near Leyden, Holland. Already at the age of eleven he had become thoroughly grounded in Latin and Greek. At about this time an ulcer developed on one thigh, and it was not until seven years later that it finally cicatrized. Every surgical measure had been tried in the hope of effecting a cure of this lesion, but all in vain; the desired result was finally obtained after the frequent employment of lotions consisting of urine to which salt had been added. The suggestion to use this extraordinary remedy was made by the boy himself, and it was doubtless the success thus obtained which led him eventually to choose medicine as his vocation. Up to 1690 Boerhaave's education was based upon the idea that he would follow the career of a theologian, but in that year he began seriously to study the anatomical treatises of Vesalius, of Fallopius, and of Bartholinus, and he also followed a course of dissection under the guidance of the anatomist Nuck. To these studies he soon added that of the practice of medicine, his favorite authors being Hippocrates and Sydenham; and, later still, he devoted a great deal of time and much thought to chemistry and botany, in both of which departments of knowledge he became thoroughly well versed. In 1693 he received the degree of Doctor of Medicine; and sixteen years later, in 1709, the University of Leyden made him Professor of Medicine and Botany. Students flocked to his lectures from all parts of Europe. His two principal treatises—the one entitled "Institutiones rei medicæ in usus annuæ exercitationis domesticæ" (Leyden, 1708), and the other "Aphorismi de cognoscendis et curandis morbis, in usum doctrinæ medicinæ" (Leyden, 1709)—furnished the basis of his lectures; and, in addition, he conducted clinical courses very much like those of the present day. As a practitioner of medicine Boerhaave was also remarkably successful, and his clientèle came from every part of Europe. A story is told that he received from a mandarin in China a letter addressed to "M. Boerhaave, physician in Europe." He died in Leyden on September 23, 1738, from an affection of the heart.

Fig. 839.—Hermann Boerhaave.

The influence exerted by Boerhaave upon the science of medicine, both during his lifetime and for many years after his decease, was very great. This influence must be attributed, not to anything specially original in his teachings, but to the clear and systematic manner in which he both wrote and spoke, and to a certain charm of manner. His knowledge of European languages is said to have been remarkable. (Dict. Hist. de la Med.)

A. H. B.

Boerne, Texas, is a town of about 1,000 inhabitants situated in the southwestern part of the State, thirty miles northwest from the city of San Antonio. Its altitude is about 1,670 feet, which gives it somewhat the characteristics of a mountain resort of moderate elevation. The soil is composed of gravel and sand with occasional streaks of adobe, and a substratum of porous limestone. The drainage is good, both on account of the slope and on account of the porous character of the soil.

Dr. I. M. Cline (Solly's "Medical Climatology," 1897), who had charge of the Texas weather service, describes the country in which Boerne lies as follows: "Between latitude 29° 45′ and 30° and to the 100th meridian on the west, the elevation changes rapidly from one thousand to two thousand feet, with considerable irregularity, and is broken with deep ravines and small creeks, and along the western border, as the two-thousand-foot line of elevation is reached, it is much sculptured by erosion. The soil between these elevations is very irregular in its formation, but is to a great extent of the black, stiff soil over the eastern portion, and then blends toward the west with black and red sand and red loam, with a pebbly soil in some parts; it is also crossed here and there by strips of white, sandy land, with a growth of scrub post-oak."

The monthly mean temperature for eight years, arranged by seasons, is given by Solly as follows: Winter, 50°; spring, 69°; summer, 79°; autumn, 65°; Mean for January, 49°; for July, 81°; for the year, 65°. The total seasonal rainfall, based on nine years' records, is given by the same authority as follows: Winter, 5.9 inches; spring, 9.6 inches; summer, 6.4 inches; autumn, 4.9 inches. Annual mean, 27 inches. The mean relative humidity is from sixty-six to seventy-two per cent. Occasionally during the winter months there is a sudden fall in temperature during the prevalence of a "norther"; this fall depends on the velocity of the wind and ranges from 5° to 25° F., and lasts from a few hours to three or four days. The windfall is light, the prevailing winds blowing from the south and southeast, the velocity ranging from four to seven miles an hour, and occasionally increasing to from fourteen to twenty-five miles during a "norther." "From the fact," says Miller ("Boerne and Adjacent Country," by Dr. William Miller, Resident Physician), "that the wind passes over miles of land covered with grass and trees before reaching Boerne, it is not accompanied with clouds of dust or sand," which, as Dr. Miller adds, is a very important matter with persons suffering from diseases of the respiratory organs.

There are a few light morning fogs in the late autumn and winter, not exceeding a total of eight days in the year. The average number of sunny days is 277, and of cloudy eighty-eight. The number of days in which there is more or less sunshine, and in which an invalid can be out of doors, is 355. In Boerne and the adjacent country there are no prevailing diseases of a contagious or epidemic nature. The whole of this elevated district is above the yellow-fever line (Miller).

The water supply is chiefly obtained from wells of an average depth of thirty-five feet, and the water is considered fairly good for drinking purposes. Cistern water is also used. About three miles from Boerne are the Indian Mineral Springs, so named from the fact that they were visited periodically by various Indian tribes, who came bringing their sick with them. This water is also used as a table water. The anal-

ysis made by C. F. Chandler, Ph.D., of New York, is as follows:

One United States Gallon Contains:	
Solids.	Grains.
Chlorine in chlorides	0.512
Equivalent to sodium chloride	.844
Oxides of iron and aluminum	.093
Lime	45.832
Magnesia	6.135
Sulphuric acid (SO_3) in sulphates	67.246
Silica	.355
Solids of evaporation	138.388

There are several fairly good hotels and boarding houses in the town or near by. Boarders are also received in the ranch houses in the neighborhood. Living is said to be inexpensive. The attractions are riding, driving, hunting, and fishing, and there are various pleasant excursions in the vicinity. The class of diseases which this climate is likely to benefit are pulmonary tuberculosis, chronic rheumatism, renal, nervous, and malarial diseases.

When one considers the low relative humidity, the equable climate, and especially the very large number of sunny days in the year (277), the inference is warranted that Boerne is admirably fitted for the open-air treatment of pulmonary tuberculosis, in the early or moderately advanced stages. While experience has verified this conclusion, the fact still remains that here, as in so many other climatically excellent health resorts in this country, there is lacking the certainty of finding such hygienic conditions as the consumptive requires. Climate is only one of the factors in the cure of phthisis, and it will often prove an illusory one unless those other factors are also present, viz., careful medical supervision and opportunities for obtaining proper food, well-ventilated sleeping apartments, and means for the rest cure. Boerne is off the beaten track and in consequence has not received such general recognition as a health resort as its excellent climate deserves.

Edward O. Otis.

Boil.—*Definition.*—A boil or furuncle is the result of an acute phlegmonous inflammation of the skin and underlying connective tissue surrounding a skin gland or follicle, which is followed by suppuration and the extrusion of a central slough or core.

Symptoms.—A boil begins with a certain amount of infiltration around a skin gland or follicle, which soon manifests itself as a small, somewhat itchy, and slightly painful pimple. Very soon the lesion assumes a conical shape, becomes more tender, and is surrounded by a zone of reddened skin. The boil increases in size with considerable rapidity until about the third or fourth day, when it reaches its full development. The pain likewise grows in intensity, becoming a dull ache, and there is much throbbing with a sensation of tension. All of these symptoms are intensified at night. The area of the furuncle varies considerably, depending upon the density of the skin in the affected part, and the consequent facility with which the infiltration may spread. Finally, at the apex of the boil a point of suppuration appears, and in a week or ten days the lesion matures or becomes "ripe." If pressure is made over a boil before it is quite mature a little pus or bloody serum may be made to exude; but later, either spontaneously or as the result of surgical interference, the core escapes, although not always very readily. The expulsion of the core exposes to view a small cavity which quickly heals, to be followed in turn by a purplish discoloration and ultimately by a minute scar. Lymphangitis and swelling of the lymphatic glands frequently occur in connection with boils, and sometimes constitutional symptoms are marked. When a core does not form, as occasionally happens, it is called a blind boil. Boils may occur singly or in groups; often they come out in successive crops, and keep on appearing for long periods, constituting the condition known as furunculosis. The so-called "furuncular diathesis," especially as seen in children, may produce great restlessness, sleeplessness, anorexia, and emaciation due to pain and the free discharge of pus. It may be of interest in this connection to mention that under the name of "hidradenitis suppurativa" Pollitzer has called attention to a suppurative inflammation of the sweat glands which results in their destruction and the production of scars. It is the same condition originally described by Verneuil.

Situation.—While boils may develop anywhere on the general surface, except the palms and soles, they show a marked predilection for the back of the trunk and neck. They also occur in the armpits and at the borders of the lids (styes) and in the external auditory canal, in which latter situation they excite great pain.

Pathology and Etiology.—It is now conceded that boils are due to the entrance of pus cocci (*Staphylococcus aureus* or *albus*) into the openings of skin glands or hair follicles. According to the researches of Bockhardt, if the microorganisms do not penetrate into the cutis, simple impetigo results; if they pass vaguely into the cutis through some lesion in the epidermis, a skin abscess will occur; but if they pass along the duct of a sweat gland or penetrate the lumen of a hair follicle, the process of suppuration is more acute and a furuncle results, the suppurating gland or duct representing the core. Direct inoculation or experimental cultures show conclusively the contagious nature of boils, as was pointed out long ago by Startin. According to Melsome, it is not possible to obtain cultures in the edematous area surrounding a boil; however, when a furuncle is large, or is rapidly followed by others in its immediate vicinity, the pus cocci pass through the abscess walls and travel along the lymphatics, producing swelling of the lymph glands, and in severe cases they may even gain access to the general circulation and induce septicemia.

It is said that women are less subject to boils than men, and that while boils are not uncommon in infants, they are most frequent in boys and young men. Solitary boils are often found to be due to some local irritation, *e.g.* chafing of rough or frayed garments, decubitus, etc., the irritated skin more readily allowing the penetration of pus organisms. A condition of furunculosis of the back of the neck is not infrequent as the result of infection from the fingers of barbers and the use of the dirty implements of their trade.

Sweaters and other garments worn by young men in training and in athletic games frequently become infected and give rise to boils in otherwise singularly healthy persons.

It is a matter of common experience that furuncles complicate many disorders of a depressing character, *e.g.* diabetes, variola, typhoid fever, etc. Severe pruritic diseases are also often complicated or followed by boils; for example, eczema in children. In the hot summers experienced in this country the very common prickly heat is frequently followed by boils, both in children and adults.

The condition known as furunculosis, or recurrence of boils in crops, is due to local reinoculation and not to the state of the blood, although it is undoubtedly true that the nutrition of the soil will have much to do with the pathogenetic action of the pus cocci.

With our present knowledge of the pathology of boils it may be readily understood how boils

sometimes occur quasi-epidemically in families and schools.

Diagnosis.—A boil is to be distinguished from a carbuncle by its conical shape and its single suppurating point; a carbuncle, on the other hand, is larger and flatter than a boil, has several openings, and is surrounded by a much more brawny induration. The difference really is one of degree, the carbuncle being, however, clinically, a much more formidable affection.

Treatment.—In all cases, especially when the eruption has existed for a long time, it is advisable, in addition to the local measures presently to be described, to look into the hygienic surroundings and general health of the patient. The urine should be examined for albumin and sugar, and if these are discovered the proper treatment for those conditions should at once be adopted. All local sources of irritation and possible infection should be diligently sought and removed. Old smoking jackets, sweaters, etc., should be regarded with suspicion. A proper disinfection of barber's tools should be insisted upon.

Now that the specific character of the furuncle is better understood there is less insistence upon the administration of the host of remedies that are supposed to be "good for boils."

Among such remedies may be mentioned yeast in doses of a half-wineglassful morning and night, and the sulphide of calcium so highly praised by Ringer. It is quite possible that the sulphide of calcium may possess some germicidal properties, but it must be given in much larger doses than those usually recommended. Dilute sulphuric acid in ten to twenty drop doses, well diluted, every three or four hours, is highly esteemed by some physicians. Medicines that improve the general nutrition, thus rendering the individual less susceptible to local infection, are of undoubted value in furunculosis; for example, iron, arsenic, cod-liver oil, the hypophosphites, and the syrup of the lacto-phosphate of lime may be prescribed with hope of benefit in suitable cases. The treatment of boils by means of the bacterial suspension, or the so-called bacterial vaccine, has in many cases proved highly satisfactory, and it is probable that in no disease is it of more value. While on theoretical grounds the autogenous preparation would seem the more desirable, results equally satisfactory are obtained with the stock suspension.

An emulsion representing a single type of the staphylococcus (*e.g. Staphylococcus aureus*) may be employed, or one containing mixed organisms.

The initial injection may contain 100,000,000 staphylococci, the dosage being increased at intervals of one week, until the injection of 500,000,000 or 1,000,000,000 is reached. A cure is usually effected within at least ten injections, and one or two may be sufficient.

As regards the direct treatment of the boil itself an effort should be made to prevent if possible, or at least limit, the suppuration. Very often a boil may be aborted by the application of a salicylic acid plaster, as after L. Heitzmann's formula:

℞ Acidi salicylici . . . 3ss.
Emplastri saponis . . 3ij.
Emplastri lithargyri . 3i.
M. S. Spread on cloth.

Other remedies of this class are iodine, boric acid in saturated solution, and ichthyol. Halle and Jamieson advise the following application:

℞ Tincturæ iodi . . . 3i.
Acidi carbolici . . . 3ss.
Pulveris talci . . . 3ss.
M. S. Apply externally.

A few drops of carbolic acid injected into the apex of a boil will often cause it to abort. An electrolytic needle will do the same thing. If a hair occupies the center of a furuncle it is best to extract it.

Unna's mercuric-carbolic plaster often succeeds in aborting a boil; but if suppuration has already begun, nothing succeeds so well in hastening it. A hole should be cut in the center of the plaster corresponding to the apex of the boil. When boils are very painful the common practice is to apply a hot flaxseed poultice, but unless it is rendered antiseptic by the addition of carbolic acid it is apt to prove mischievous by favoring reinfection in the vicinity. The following ointment serves all the purposes of a poultice, does not encourage reinfection, and allays pain most decidedly:

℞ Xeroformi . . . gr. xlviii.
Vaselini,
Lanolini . . . āā 3j.
M. S. Spread on patent lint.

Bowen recommends the following ointment as a suitable application spread on cotton or lint and kept in place by a bandage.

℞ Acidi borici,
Sulphuris præcip. . . āā 3i.
Vaselini . . . 3i.
M. S. Spread on lint.

The internal administration of appropriate doses of acetphenetidin will usually secure sleep at night. If incisions are imperatively demanded the parts may be rendered insensible by a spray of ethyl chloride. It is an absolute necessity, especially where boils are multiple, to smear the intervening and surrounding skin with a paste made of equal parts of oxide of zinc and vaseline and four-per-cent. boric acid. Washing the skin with green soap and warm water and mopping on a solution of bichloride of mercury 1 to 1,000 often puts a stop to reinoculation. Clean underclothes should be put on frequently and the patient warned against carrying infection to other parts with his fingers. Squeezing and other manipulation of a boil should be avoided. After the boil has burst the resulting cavity should be treated on ordinary surgical principles. W. A. Hardaway.

Boldo.—The leaves of *Peumus boldus* Molino (fam. *Monimiaceæ*). This is a large, much-branched shrub or small tree of Chile, evergreen and highly aromatic, the leaves opposite, the flowers small, white, panicled, diecious. The leaves usually dry of a brownish color. They are coriaceous and very thick, ovate or ovalovate, blunt or emarginate, entire, rough, papillose, and stellate-hairy. They contain numerous large oil vesicles, and have a strong, somewhat turpentine-like odor and an aromatic, burning taste.

Boldo contains about two per cent. of a powerful volatile oil, with resin, a little tannin, three per cent. of the glucoside boldin or boldoglucin and one-tenth per cent. of the alkaloid boldine. The statements concerning the properties of the constituents are very discordant. According to Merck, the hepatic properties reside in the glucoside, the dose of which is 0.065 to 0.2 gram (gr. i. to iij.), and the hypnotic properties in the alkaloid, the dose of which is 0.002 to 0.0065 gram (gr. $\frac{1}{30}$ to $\frac{1}{10}$).

The properties of the leaves are very marked, and it seems strange that the drug should not have acquired a higher repute. Its original use was that of an alterative, with special reference to the liver. Marked sedative properties were encountered, and it has been considerably used as a hypnotic in insomnia. For the latter purpose the dose should be two to four grams (3 ss. to i.), for the former a fourth as much. The drug should be systematically investigated. It is now very little used. H. H. Rusby.

Bolus.—A bolus is a pill-like mass, containing medicinal agents; it is larger than a pill, generally

weighs from five to ten grains, is used chiefly in veterinary practice. The bolus is not official in either the U. S. P. or the B. P. When sugar-coated, the bolus is called a dragée. R. J. E. S.

Bonduc.—*Bonduc Nut; Nicker Tree.*

The seeds of *Cæsalpinia bonducella* (L.) Roxb. and of *C. bonduc* Roxb. (fam. *Leguminosæ*).

These plants are not only abundant in India, where they are native, but have been very largely introduced to most tropical countries. The seeds have the shape of a smooth pea, but are one-half or three-fourths inch in diameter, and smooth and shining. Those of *C. bonducella* are of a peculiar gray lead-color, those of *C. bonduc* yellowish-brown. The former especially are classical in the medical history of India, the uses being numerous and varied, and some of them doubtless ignorant. Its chief reputation appears to have been in the treatment of malaria, and careful trial has shown it to possess antiperiodic properties of some importance. The seeds contain twenty-five per cent. of fixed oil, which has been expressed and used like other fixed oils. They also contain about two per cent. of an amaroid, which is a white powder, and apparently the active constituent. Like all seeds of their class, they are rich in protein. The shell contains tannin. The antiperiodic dose of the bitter principle is 0.1 to 0.2 gram (gr. iss. to iij.).

H. H. Rusby.

Bone, Chemistry of.—See *Cartilage, Bones, and Teeth, Chemistry of.*

Bone, Histology and Development of.— Bone tissue is closely allied in genesis and in many of its structural features to the other members of the connective-tissue group, the most evident difference between it and other tissues of the same class consisting in the solidity and firmness of the basement substance. For in this, as in other connective tissues, we have to consider the cells and the basement substance and the way in which they are arranged to form the different varieties of tissue. The solidity of the basement substance of bone depends largely upon the deposition within it of calcium phosphate and carbonate, with small amounts of calcium fluoride, sodium chloride, and salts of magnesium. These inorganic salts, which form about two-thirds of the weight of the bone, are deposited in an organic matrix in such a condition of minuteness that they are not recognizable as particles even with high powers of the microscope. They may be dissolved out of the bone with dilute acids, leaving a translucent flexible material behind, which preserves the shape and general structural features of the bone.

The soft matrix which is left after the extraction of its inorganic salts may be converted into gelatin by boiling in water. It is sometimes called the cartilage of bone, or ossein; but there is no sufficient reason for using these names, since the matrix is really, both in chemical nature and in minute structure, closely allied to the basement substance of fibrillar connective tissue.

The varied gross appearances which different bones or different parts of the same bone present have given rise to the names *compact bone tissue* and *cancellous bone tissue* or *spongy bone*. But the essential structure of the tissue is the same in both, the difference consisting largely in the arrangement of the bone tissue proper, and its abundance in proportion to the marrow spaces or vascular canals which it encloses. The compact bone tissue is in general found in the outer portions of the bones, while the cancellous tissue is situated internally, either entirely filling the central portions or bordering the marrow cavities.

Bones are surrounded by a layer of vascular connective tissue called the *periosteum*, and contain, either in large central cavities or in the smaller spaces with which they are everywhere permeated, a delicate vascular tissue called *marrow*. We have, then, to consider: 1. bone tissue proper; 2. the periosteum; 3. the marrow.

1. *Bone Tissue Proper.*—If we remove the inorganic salts from one of the long bones, by soaking it in dilute chromic or picric acid (see article on *Histological Technique*), and then make a thin longitudinal section, microscopical examination with a low power of these sections, stained with eosin and mounted in glycerin, reveals a picture like that represented in Fig. 840. The more solid portions of the bone show a series of narrow canals, running in a direction in general parallel with the long axis of the bone, and in frequent communication with one another by similar short transverse or oblique canals. These are the so-called *Haversian canals*, and contain blood-vessels, and, depending upon their size, few or many variously shaped cells. Along these Haversian canals the basement substance will be seen arranged in a series of lamellæ, while in and between these lamellæ lie small, elongated cavities

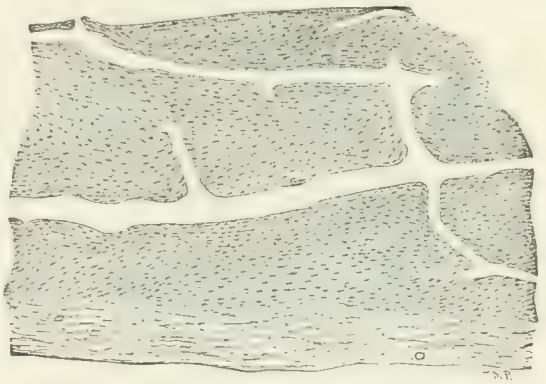

Fig. 840.—Longitudinal Section of Human Tibia, Decalcified and Mounted in Glycerin. (× about 20 and reduced.)

called lacunæ, in which are the bone cells. Transverse sections, however, through the middle of a long bone, reveal with more distinctness the arrangement of the lamellæ of the basement substance (Fig. 841). The Haversian canals, which are cut transversely or obliquely across, are surrounded by a series of concentric lamellæ. These Haversian lamellæ, with their enclosed lacunæ, together with the canals and their contents, form the so-called *Haversian systems*. Filling the larger and smaller irregular areas between the Haversian systems are other parallel lamellæ, which run in various directions, and which are called *intermediary systems*. Beneath the periosteum, at the external surface of the bone, is a thinner or thicker system of lamellæ called *circumferential* or *general lamellæ*, which cover over large numbers of the Haversian systems and surround the entire bone. Sometimes similar but less well-defined general systems of lamellæ border the marrow cavity, but more often the internal surface of the compact bone is beset with a series of projecting bony trabeculæ, consisting of lamellæ similar to those forming the systems of the compact bone, and inclosing large, irregular spaces. This is the cancellous tissue bordering the marrow cavity. In the heads of long bones, and in most short or irregular-shaped bones the cancellous tissue occupies the entire central portion.

If, now, we study more closely the minute structural features of the bone, we find in the first place that the Haversian canals, as seen in transverse sections of the bone, vary considerably in size and shape. Some are large, others small; some are round, others oval, others irregular in shape. In many cases, however, the oval shape of the Haversian canals and of their systems of lamellæ appears to be due to the obliquity of the

section. In some cases the canals lie in the center of the systems, in others near the side. Sometimes the Haversian systems are complex, one set of concentric lamellæ seeming to have encroached upon the space formerly occupied by another (Fig. 841). Furthermore, the borders of many of the Haversian systems, where these abut on one another or upon the intermediary systems, appear scolloped or jagged. This appearance will be explained below, when we consider the growth of the bone.

Turning now to the bone cells and the spaces in which they lie—the lacunæ—we find that some other mode of preparation is necessary than that of mounting sections of decalcified bone in glycerin, because the whole extent of the cell spaces is not revealed, on account of their partial filling by the mounting medium.

If, however, we take a bone which has been macerated and dried, to remove the fat and other soft

Fig. 841.—Transverse Section of a Bone (the Ulna) Deprived of Its Earth by Acid. (Sharpey.) Magnified 20 diameters. Haversian systems of canals and concentric lamellæ.

tissues, and prepare thin sections by grinding and polishing them, and then mount them in hard balsam, which is melted, and, after the section is enclosed, cooled so quickly that it does not have time to penetrate far into the tissue, the full extent of the cell cavities is revealed. For all the spaces are now filled with air, which gives them a dark appearance by transmitted light. In a section thus prepared (Fig. 842), it will be seen that the lacunæ are elongated, mostly fusiform, irregular cavities, lying between and in the lamellæ, and that from these minute branching canals, called *canaliculi*, pass off, piercing the lamellæ and forming frequent communications with the canaliculi of neighboring lacunæ. The canaliculi which pass out from the lacunæ lying near the Haversian canals pierce the walls of the latter and open into them. The canaliculi of neighboring Haversian systems, however, do not, as a rule, communicate with one another.

In the lacunæ, as may be seen in carefully prepared thin sections of decalcified bone, lie the flattened and, in some cases, branching bone cells. To what extent the branches of the cells pass into the canaliculi is not yet fully established. The bone cells have large nuclei and finely granular bodies.

According to von Ebener, Sharpey, and others, the basement substance of bone is not homogeneous, but is permeated by exceedingly minute decussating fibrils, similar to those of the basement substance of ordinary fibrillar connective tissue. Certain of the

Fig. 842.—Transverse Section of Compact Tissue of Humerus. Magnified about 150 diameters and then slightly reduced. (Sharpey.) Three of the Haversian canals are seen, with their concentric rings; also the lacunæ, with the canaliculi extending from them across the direction of the lamellæ. The Haversian apertures had become filled with air and débris (from the grinding), and therefore appear black in the figure, which represents the object as viewed with transmitted light.

lamellæ, particularly those of the circumferential and intermediary systems, are pierced by bundles of delicate fibrils, which pass perpendicularly or obliquely through them. These fiber bundles, called *Sharpey's fibers*, may be seen projecting from the inner side of small bits of bone torn forcibly away from one another, near the surfaces of decalcified

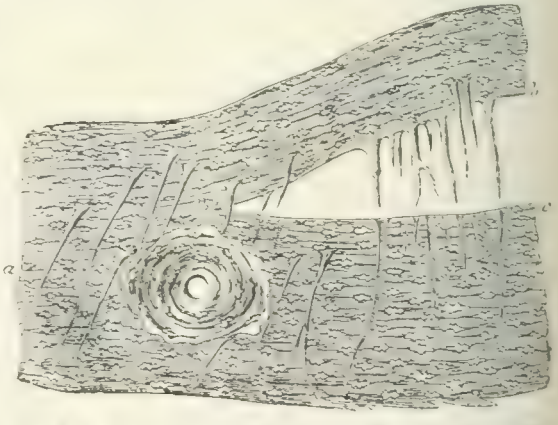

Fig. 843.—Section through the External Table of a Decalcified Human Parietal Bone. *a*, Sharpey's fibers in their natural position; *b*, fibers which have been pulled out of the underlying basement substance, *c*. (After H. Muller.)

bones (Fig. 843) as well as in very thin sections. These Sharpey's fibers, as will be seen when we come to the development of bone, are the remains of the old fibrillar connective-tissue matrix in which the bone is formed.

During the past ten years and even much earlier attempts have been made to distinguish histologically human compact bone from the same tissue when of animal origin. In 1910, W. Geyer wrote a graduation thesis (Jena) on this subject. The differences must, of course, lie in the Haversian systems of the respective animals including man, as shown in cross-section. Attempts at differentiation have been based on the number and width of the Haversian lamellæ, the number, size and grouping of the bone-corpuscles, the distances between the Haversian canals, etc. That notable differences exist among the bone tissues of certain species of animals is very evident, as is also the fact that all these tissues tend to follow some particular type of Haversian system. But thus far no such distinctions have been established as would serve for forensic ends, despite allegations to the contrary (Geyer).

2. *The Periosteum* is a fibrous sheath surrounding the bones, except over their articular surfaces. It consists of moderately dense layers of fibrillar connective tissue containing numerous blood-vessels, which ramify in the outer portions and finally enter the bone through the Haversian canals. There is a considerable number of elastic fibers in the inner portions of the periosteum, and it contains an abundant system of lymphatic vessels. In the growing bone irregular layers of large granular cells, called osteoblasts, lie in the inner layers of the periosteum, and between it and the bone. The periosteum contains a few nerves, which chiefly pass from it into the bone tissue.

3. *The Marrow* is a complex tissue which fills the large central cavities in the shafts of the long bones, the spaces in the cancellous tissue, and the larger Haversian canals. Marrow tissue varies considerably in its appearance and structure in adults and in the young, as well as in different bones in the adult. In the adult the marrow in the shafts of long bones consists of blood-vessels and a delicate connective-tissue reticulum which supports a great abundance of fat cells and a varying number of small spheroidal cells scattered between the fat cells. Such marrow has a yellow appearance from the fat which it contains.

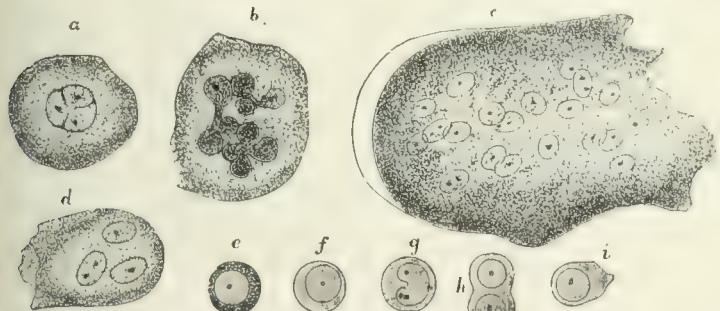

Fig. 844.—Cells of the Red Marrow of the Guinea-Pig. Highly magnified. (Schäfer.) *a*, A large cell the nucleus of which appears to be partly divided into three by constrictions; *b*, a cell the enlarged nucleus of which shows an appearance of budding into a number of smaller nuclei; *c*, a so-called giant cell or myeloplaxe with many nuclei; *d*, a smaller myeloplaxe with three nuclei; *e–i*, proper cells of the marrow.

In the cancellous tissue of both long, irregular-shaped, and short bones in the adult, and in all of the bones in young animals, the marrow is red in color, and contains comparatively few fat-cells. Red marrow consists, like the yellow marrow, of blood-vessels, lymph vessels, and a delicate reticular framework whose meshes are more or less filled with cells. These cells are of several kinds (see Fig. 844). There are abundant small spheroidal cells with nuclei, which are very large in proportion to the size of the cell body; and between these and considerably larger cells, also with large and often irregularly shaped and sometimes double nuclei, there are numerous intermediate forms. All of the above forms are very abundant in red marrow, and constitute the *marrow cells* proper (Fig. 844). Then we find, much less frequently, and in varying numbers in different bones of the same animal, and in the bones of different animals, much larger, usually multinucleated cells, the so-called *myeloplaxes* or giant cells (Fig. 844). These myeloplaxes, although always large, vary considerably in size and shape, and in the number of their nuclei. The nuclei are apt to be collected in a compact mass near the center of the cell, and often present quite bizarre and indescribable shapes. Finally, red marrow contains, in varying number, small nucleated cells, which bodies have the color and general appearance of red blood cells, the so-called *nucleated red blood cells*, and small spheroidal cells whose bodies contain larger and smaller particles of pigment, and a moderate number of fat cells.

The Development of Bone.—It will be possible within the limits of this article to give only a very brief general description of the somewhat complex way in which bone is formed. It is customary to describe the development of bone as occurring in three ways, or, speaking more correctly, to describe three phases of bone development. These are *intracartilaginous*, *intramembranous*, and *subperiosteal*. It should be borne in mind, however, that the essential nature of the process is the same in all.

Intracartilaginous Ossification.—Most of the long and irregular-shaped bones in the body consist, at an early period of life, of masses of hyaline cartilage, which present, in a general way, the shape of the future bone. The transformation of these cartilage masses into bones is intracartilaginous ossification. This is always associated with a certain amount of subperiosteal ossification in the manner to be described below. Macewen ("Growth of Bone," 1912) insists that the periosteum is not an osteogenetic structure, and that there is no evidence that it either produces or reproduces bone. It is only a limiting membrane which prevents the highly vegetative osteoblasts from invading the surrounding tissues during development. Bone does not die because bereft of periosteum and bare bone is not necessarily dead bone. Subperiosteal ossification is, of course, an assured fact, but according to Macewen the periosteum plays no active rôle therein. It only provides by its protection and limitation a suitable nidus for the genesis of the external lamellæ of bone.

If we look at one of the cartilage masses which is to be converted into a long bone—at one of the bones of the finger or toe, for example (Fig. 845)—at a period when the process of ossification is about to commence, we notice that at the central portion of the mass the cartilage cells are larger than in other parts, and closer together, and that the basement substance between them is finely granular from the deposition in it of salts of lime. While this preliminary calcification of the cartilage and the enlargement of its cells are going on, a shell of bone is forming around the middle of the shaft beneath the periosteum, and as the cartilage near the ends continues to grow and expand at the sides, the entire mass assumes somewhat of an hour-glass shape. Now the blood-vessels from the perichondrium—which has become a periosteum on account of the above-mentioned shell of bone which has been formed around the shaft—begin to advance in the central portion of the cartilage, and this becomes channelled out in irregular branching canals in the region of

the enlarged cartilage cells, so that after a time a considerable portion of the central part of the shaft of the bone is permeated by a series of vascular canals. The general appearance of the bone at this time is seen in Fig. 846.

A closer examination at this period will show: (1) that the cartilage cells which lie in the region just beyond the advancing vascular canals have assumed a peculiar arrangement and are large; (2) that the basement substance of the cartilage in the same region is calcified; and (3) that thin layers of new bone are beginning to form along the edges of the vascular canals in the central portion of the shaft.

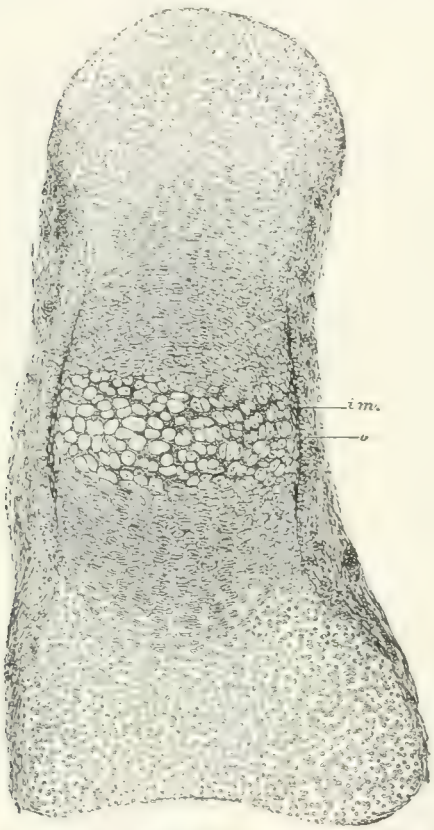

FIG. 845.—Section of Phalangeal Bone of Human Fetus, at the Time of Commencing Ossification. (Schäfer.) The cartilage cells in the center are enlarged and separated from one another by dark-looking calcified matrix; *im*, layer of bone deposited underneath the periosteum; *o*, layer of osteoblasts by which this layer has been formed. Some of the osteoblasts are already embedded in the new bone as lacunæ. The cartilage cells are becoming enlarged and flattened and arrayed in rows above and below the calcified center. At the ends of the cartilage the cells are small and the groups are irregularly arranged; the fibrous periosteum is not sharply marked off from the cartilage.

If we look at a similar bone at a somewhat later period, we find that while a layer of subperiosteal bone tissue of considerable thickness has been formed round the shaft, the central portions of the structure are also filled with irregular bony trabeculæ, between which lie the vascular canals or marrow cavities (Fig. 846); and, furthermore, that the cartilage cells toward the ends of the bone, in the region just in front of the advancing marrow cavities, are, as before, large and arranged in rows and lie in a calcified basement substance.

It is now necessary to look more closely at the changes in the cartilage which precede the ossification, and to study the exact way in which bone tissue is formed along the walls of the advancing marrow cavities.

If we look with a high power at a thin section of a carefully preserved and decalcified bone in the process

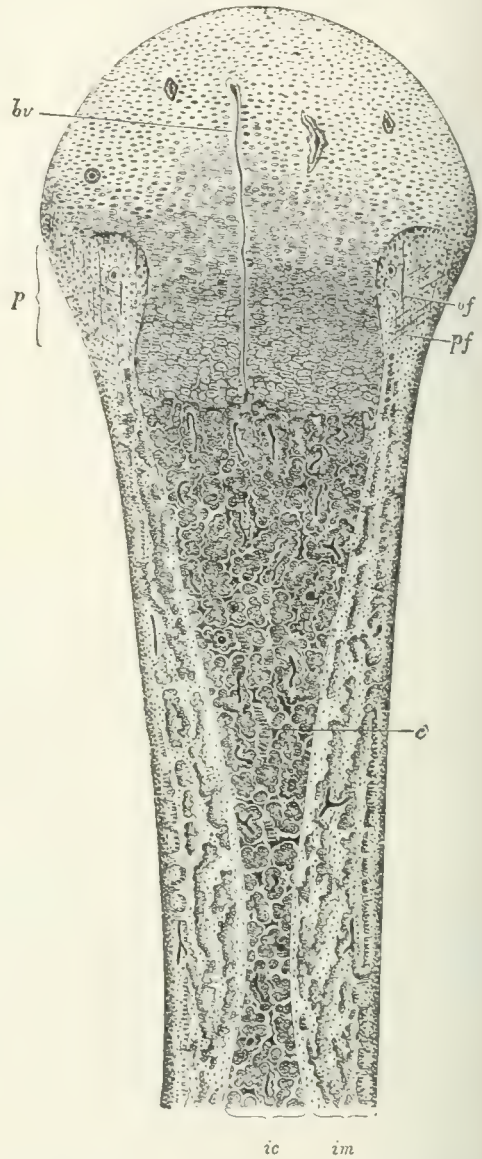

FIG. 846.—Longitudinal Section through the Upper Half of the Decalcified Humerus of a Fetal Sheep. Magnified about 30 diameters. (Schäfer.) *ic*, The part of the shaft which was primarily ossified in cartilage. One long, straight vessel (*bv*) passes in advance of the line of ossification far into the cartilaginous head; most of the others loop round close to the cartilage. At one or two places in the older parts of the bone, elongated groups of cartilage cells (*c*) may still be seen which have as yet escaped absorption; *im*, the part of the bone that has been ossified in membrane, that is to say, in the osteoblastic tissue under the periosteum. The subperiosteal layer is prolonged above into the thickening (*p*), which encroaches upon the cartilage of the head of the bone, and in which are seen, among numerous osteoblasts and a few blood-vessels, the straight, longitudinal osteogenic fibers (*of*), and some other fibers (*pf*) crossing them, and perhaps representing fibers of Sharpey.

of development, confining our attention for a moment chiefly to that region which lies along the ends of the above-described advancing marrow cavities, and

for a short distance on either side, we find a condition similar to that represented in Fig. 848. At some distance toward the end of the bone from the medullary cavities the cartilage cells become flattened and are arranged in irregular rows, *b;* nearer the ossifying portions of the bone the cartilage cells are larger and more closely packed together; and finally, just beyond the ends of the advancing marrow canals, large cartilage cells are seen lying in elongated cavities in the basement substance, *c.* Each cavity contains several cells, which, in many cases, are separated from one another by narrow partitions of cartilage basement substance. Here and there along this region it will be seen that the marrow canals with their contained blood-vessels have opened into and become continuous with the spaces containing the large cartilage cells, and the latter have either disappeared or have assumed some different form. This occurs sooner or later, and usually at about the same time, all along this region, so that the advancing blood-vessels convert the spaces originally containing cartilage cells into vascular canals or marrow cavities.

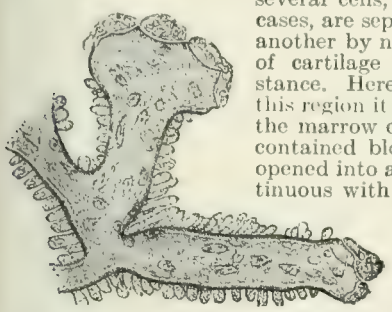

FIG. 847.—Bony Trabecula from the Lower Jaw of a Calf Embryo, with Howship's foveolæ and giant cells at the ends where absorption is proceeding and osteoblasts covering the sides where bone is being deposited. (Kölliker.)

If we look now at the region near the ends of the marrow canals, we find that these canals contain thin-walled blood-vessels, numerous small spheroidal cells, and larger cuboidal, ovoidal, or fusiform granular cells, which are apt to be arranged along the sides of the canals. These latter cells are the so-called *osteoblasts,* under whose influence the bone tissue is formed.

The exact way in which the bone tissue is deposited under the influence of the osteoblasts may be readily seen in very thin sections through the zone of ossification, which have been stained double with hematoxylin and eosin (see article on *Histological Technique*) and mounted in balsam. A small portion of such a section made transversely across the bone is represented in Fig. 847. Just beneath the osteoblasts which lie along the edges of the marrow canals thin crescentic shells of strongly refractile calcareous material—the basement substance of bone—are formed. These shells grow thicker and thicker, and rise up around the sides of the osteoblasts. They are pierced by delicate canals, which are to form the canaliculi. Gradually the entire osteoblast, which has become somewhat flattened and jagged in outline, is enclosed by the bony basement substance and becomes a bone cell. This process goes on around the osteoblasts, which lie side by side all along the walls of the marrow spaces, so that the latter are presently enclosed by an irregular wall or encasement of new bone. Upon this, new layers are deposited, so that gradually the marrow spaces grow narrower and narrower, and finally contain only blood-vessels and a few marrow cells. This gradual bony thickening of the walls and narrowing of the marrow spaces may be seen by following the tissue in a longitudinal section from the line where ossification commences, near the distal ends of the marrow spaces, toward the center of the bone where the process is oldest.

The fragmentary remains of the old basement substance of the hyaline cartilage persist for some time, surrounded by the new-formed bone: but they grow smaller and smaller as more bone is formed, and are finally absorbed and altogether disappear.

Thus the ossification of the cartilage advances toward their ends, preceded always by a rearrangement and proliferation of the cartilage cells, and by calcification of its basement substance. What the exact purpose is of the temporary calcification of the cartilage basement substance just in advance of the ossification line we do not know, nor is it certain what becomes of the cartilage cells when the vascular canals finally open into the spaces in which they lie. Some observers believe that they disintegrate and are absorbed; others, that they become osteoblasts, or other marrow cells. Equally uncertain is the origin of the osteoblasts, and the consideration of the more or less well-founded conjectures as to their genesis would lead us beyond the scope of this article.

After a time new centers of ossification are formed near the ends of the long bones, in the epiphyses, from which bone formation proceeds in the manner above described. At length the zones of ossification in the epiphyses and diaphyses approach one another, and are separated only by a narrow band of cartilage, which finally itself becomes ossified, and the epiphysis and diaphysis are joined to form a single bone.

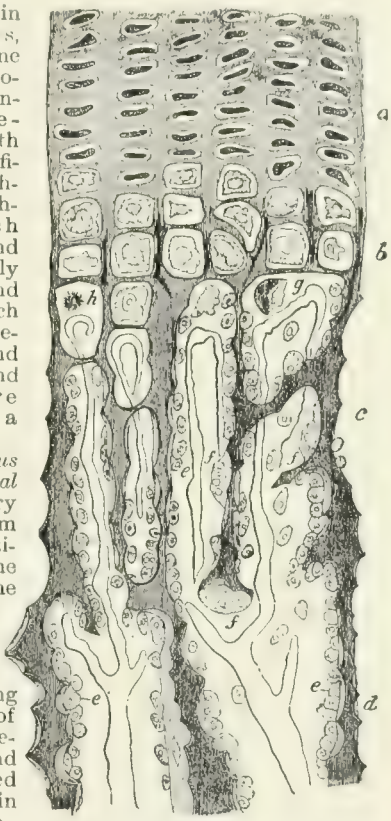

FIG. 848.—Part of a Longitudinal Section of the Developing Femur of the Rabbit. Magnified about 350 diameters. (Klein and Noble Smith.) *a,* Rows of flattened cartilage cells; *b,* greatly enlarged cartilage cells close to the advancing bone, the matrix between being partly calcified; *c,d,* already formed bone; the osseous trabeculæ being covered with osteoblasts (*e*), except here and there, where a giant cell or osteoclast (*f*) is seen, eroding parts of the trabeculæ; *g, h,* cartilage cells which have become shrunken and irregular in shape.

Intramembranous and *Subperiosteal Ossification* vary only in details from the intracartilaginous. In the former case, the tissue in which bone is to form is fibrous and vascular; osteoblasts appear along the bundles of fibers which become calcified, and bone is formed around them in the above-described manner. Some of the fibrous bundles persist within the new-formed bone, as Sharpey's fibers. The bone tissue which is at first formed is arranged in irregular trabeculæ, which cross and interlace as did the connective-tissue fibers which it replaces, and encloses irregular vascular spaces or marrow cavities, which become smaller and smaller as successive layers of bone are formed around their sides. After a time the irregular trabeculæ and their enclosed marrow spaces become covered in by more uniform layers of bone. These, in the long bones, are the circumferential lamellæ, and

in the flat bones, such as those of the skull, are the compact external and internal tables which enclose the diploë.

A pure intramembranous ossification is seen in the early stages of the formation of the flat bones of the skull. The subperiosteal ossification, on the other hand, occurs as above indicated, simultaneously with the intracartilaginous formation in the long bones, as well as at a later stage in the formation of bones which are originally laid down as membranes.

Growth of Bone.—The growth of bones when they are once formed, either in membranes or cartilages or beneath the periosteum, is a somewhat complex process. They increase in thickness by a continued subperiosteal ossification. The increase in length of long bones goes on by the ossification in cartilage until, as above stated, the epiphysis is finally joined to the diaphysis.

The large central marrow cavity of long bones, which in the adult bone is itself much larger than the entire bone at an early stage of development, is formed by the absorption of the earlier developed intracartilaginous and subperiosteal bone. This absorption occurs under the influence of large, irregular-shaped, frequently multinuclear granular cells, called *osteoclasts*. Around these cells, as they lie against the bone tissue, the latter becomes absorbed in some way, so that little pits are formed in which they lie. These pits or depressions, which are of various sizes and shapes, are called *Howship's lacunæ*. On the side of the osteoclasts which lie against the bone there is, according to Kölliker, a shining striated border. The exact nature of the influence by which the osteoclasts induce the absorption of the bone is not well understood.

Not only are the central marrow cavities formed under the influence of the osteoclasts, but by an absorption of the bone in various places, and a subsequent new formation of it over the absorbed surfaces, a remodeling of the bone may occur, inducing the various changes in shape which growing bones present. This process of absorption and redeposition of bone goes on, not only on the surfaces, but in the substance, even of compact bone, during early and adult life, inducing the minor changes which occur at this period. The intermediary systems of lamellæ, above described, as seen in transverse sections of long bones (Fig. 848), are, in many cases at least, the remains of older lamellæ which have been partially absorbed; the absorption spaces having been afterward filled in by new Haversian systems. What the conditions are whose fulfilment determines now an absorption and again a new formation of bone, or exactly what the origin of the osteoclasts is, and what their relation to the osteoblasts, we can, in the present state of exact knowledge, do little more than conjecture.

Consult, for the bibliography of the histology, development, and growth of bone, Quain's "Anatomy," vol. i., part ii., tenth edition, and the "Index Catalogue of the Library of the Surgeon-General's Office, U. S. A."

T. Mitchell Prudden.

Bone, Inflammation of.—Inflammation of bone may be induced by simple traumatism—as a fracture or stripping away the periosteum, by thrombosis or embolism of a nutrient artery, by extension from a periostitis, by extension from arthritis, by exposure to cold or to the action of certain poisons—as phosphorus and mercury, by syphilis, by pressure—as the rarefying osteitis of aneurysm, by the eruptive fevers, and especially by typhoid fever. While these fevers may possibly act as primary causes, it is quite certain that they predispose to the development of an osteitis. Lastly, certain germs play an important part in the causation of an osteitis. They are either introduced through compound injuries, or else they are carried to the bones by way of the circulation. The emphasis which should be laid upon this last factor in the causation of osteitis cannot be exaggerated.

Osteitis.—It is of little clinical value to classify the inflammations of bone, from an anatomical standpoint, into osteitis, osteomyelitis, and periostitis, since primary periostitis, with the exception of the traumatic and the syphilitic varieties, is very rarely observed; and, on the other hand, every case of myelitis leads, sooner or later, either rapidly or slowly, to involvement of the periosteum in the inflammatory process.

Regarding the firm bony substance itself, when compared with the marrow and the periosteum, it may be truly said not to take any active part in inflammation; and therefore osteitis, in a narrower sense of the word, as compared with myelitis and periostitis, is unimportant. The firm bone, however, is passively affected, as we shall subsequently notice; and clinically the death of the bone, or of a part of it, may prove to be an affair of the greatest gravity. So much is this true that it has been customary to study acute osteitis under the title of one of its most frequent results—necrosis—and a certain form of chronic osteitis under the heading of caries.

Periostitis.—Periostitis, like osteomyelitis, may originate from traumatism, either simple or compound, and in character may be simple (that is, aseptic) or septic (from the presence of microorganisms). The syphilitic variety of the disease should be classed under this latter heading, its microbic cause being the spirochæta pallida. The periosteum is first affected during the secondary stage of syphilis, that is, the stage of invasion following the incubation of the syphilitic virus in the system. Those bones which are subcutaneous seem especially liable to periostitis—for example, the tibia, sternum, and ulna; but the others are not exempt. In severe cases there sometimes appears to be a simultaneous involvement of most of the bony sheaths of the body, with consequent almost unbearable osteocopic pains. These pains are distinctly worse at night, and seem to be increased by warmth; but I am inclined to think that sufferers from osteitis and periostitis of other than syphilitic origin also complain most at night.

The syphilitic periosteum is quite tender, and I have many times noticed pitting on pressure. In this disease it is rare for the periosteum to become separated from the bone by exudations; and consequently necrosis, from failure of the superficial blood supply, is very infrequent in this form of periostitis.

In the later or "tertiary" stages of syphilis, nodes, usually flat, and of sharply defined extent, sometimes make their appearance. They are caused by infiltration of the periosteum with small round cells, and, like all gummata, tend to soften and break down. Their course, and the probability of bone involvement, seem influenced for the worse if the medical attendant, finding fluctuation, use the knife instead of rapidly pushing the iodides or other appropriate medicines. Should a gumma be opened, the best mode of handling it thereafter is to remove as much of the broken down tissue as possible and then swab the walls of the cavity very thoroughly with tincture of iodine and provide drainage.

In acute periostitis, when accompanied by free exudation of fibrin, serum, and pus, the cortical lamellæ of the Haversian systems may be separated from their vascular supply; and unless the surgeon promptly realizes the state of affairs, and makes free incisions down through the dense, unyielding periosteum to the bone, a necrosis of more or less superficial character may, and often does, result.

The clinical picture of acute periostitis is best studied, as it will be later, together with osteomyelitis; for these two diseases are commonly associated together.

A rather rare concomitant of an acute osteo-

myelitis, usually of a mild type, is a periostitis with exudation of a simple serous character between the periosteal sheath and the bone. Because of the abundance of albumin in this fluid, Ollier here adopted the tile of "osteitis albuminosa."

Chronic, non-infective periostitis may be either fibrous or ossifying in character. In the former there is much increase in the amount of connective tissue, and the thickened membrane adheres usually closely to the bone. In the latter we have as a result an ossific deposit, which may go on increasing for months or even years, ultimately producing exostoses or osteophytes. The new bone of inflammatory origin is not deposited in a regular system of lamellæ, probably owing to faulty nutrition; and it is sometimes absorbed, and disappears, the abnormal activity of the osteoblasts ceasing. This variety—ossifying periostitis—may be associated with either rarefying or condensing osteitis.

With regard to tuberculous periostitis I may state that it is especially apt to appear in the subjects of the so-called scrofulous diathesis, and in the poorly nourished, and to be accompanied by tuberculous osteitis. The discussion of its symptoms, course, and treatment need not be dissociated from that of the latter disease.

Osteomyelitis.—The terms osteitis and osteomyelitis will here be considered as one. Where the vascular changes greatly predominate, where pus, fibrin, and serum are abundantly produced, where the brunt of the inflammation is felt by the marrow and contents of the Haversian spaces, the latter term may be applied with especial propriety. And, on the other hand, those cases in which changes in the firm bony structure itself form the prominent feature, may properly be designated as cases of osteitis. However, the two go hand-in-hand. Changes in the relative density of the bony structure can occur only through cellular activity in the marrow spaces and vascular canals, and in the canaliculi and lacunæ. These changes are of two kinds: osteoporosis, or rarefying osteitis, and osteosclerosis, or condensing osteitis. In the former the character of the bone changes from compact to cancellous, and if the process continue the bone may even entirely disappear, its place being taken by a mass of granulation tissue. This variety of osteitis is very common. It is one of the essential phenomena in tuberculous osteitis; it is the process by which the rough, ossified callus following fractures is rounded off; and when a bone is subjected to pressure—as by a growing aneurysm—it is a rarefying osteitis by which it is eroded.

In osteosclerosis on the other hand, the bone grows more compact, and may even—as may be observed in some exostoses—become as dense as ivory.

It often happens that both osteoporosis and osteosclerosis are going on at one and the same time in different parts of the same bone: an osteoporosis within, for example, and an ossifying, even condensing, periostitis externally; and as a result the bone may become widely expanded, although it is a mere shell filled with granulations or with inflammatory deposits.

Or, again, following an osteoporosis, the opposite process may be inaugurated, and the cavities caused by the former morbid process may become filled with new bony deposit, perhaps of even abnormal density. We do not yet know why inflammation of bone terminates sometimes in one and sometimes in the other of these conditions. It is supposable that in condensing osteitis the osteoblasts have an undue activity. In rarefying osteitis the absorption of bone is thought by some pathologists to be caused by the presence of certain large, multinucleated cells—the myeloplaxes of Robin; cells which are also by reason of the power which they are supposed to possess called osteoclasts. In subacute osteomyelitis ragged holes, opening from the marrow spaces and Haversian canals, are formed in the solid bone. These cavities are known as the caverns or lacunæ of Howship. They contain many of the so-called osteoclasts, which, if not the cause, are certainly the witnesses of the osteoporosis.

Other pathologists repudiate the idea that these large cells posses any such power, and attribute the absorption to the influence of the new granulation tissue which is present in these cases, and which lies in contact with the bone. In agreement with Billroth they hold that just as a granulating synovial fringe erodes the articular cartilage against which it rests, "like ivy climbing over a ruin," so here in bone the granulations possess a similar disintegrating power.

In acute osteomyelitis the vascular changes are of the deepest import, since obstruction of the nutrient arteries means death of the bone *en masse*. Let us study the common cases of apparently spontaneous origin. Here the marrow tissue is at first of a deeper red, from intense congestion. Sometimes it is mottled with hemorrhagic spots. Later, a grayish hue appears, due to the presence of great numbers of pus cells; and occasionally little medullary abscesses develop. In bad cases not only does thrombosis of the nutrient vessels occur, but gangrene of the marrow and of the contents of the Haversian canals also takes place, with rapid liquefaction. The bone cells being no longer nourished die. The infection may spread rapidly, involving the whole length of the bone, or, in the milder cases, it may remain limited to a comparatively small area.

Usually the process begins in the bone, and extends thence along the course of the nutrient vessels to the periosteum, which then becomes involved. Some surgeons think that the infection spreads also through the canaliculi from bone cell to bone cell, and from center to surface.

Sometimes the reverse is the case, the periosteum being first attacked. Inflammatory products—pus, fibrin, and serum—rapidly strip the swollen and edematous periosteum from the bone, inducing the most frequent form of necrosis, that of the superficial lamellæ.

The pressure caused by the exudations is very great; so much so that fat contained in the medullary tissues may be forced out, and can sometimes be seen in globules upon the surface of the pus (Roser).

The pus finally breaks through the periosteum at some point of softening and disintegration; it enters the intermuscular connective tissue, and may finally reach the surface. In that case the pus can sometimes be seen to pulsate from its contact with the richly vascular medullary substance.

When the osteomyelitis is near a joint, the articular lamella may become involved by extension; perforation through the cartilage may occur at some point, and the most dreadful arthritis ensue. In the very young, separation of the epiphysis from the shaft may, after a week or two, occur. The cartilaginous epiphysis, from its comparative lack of vascularity, is not so subject to attack as is the adjacent bone; yet even this may die.

Those parts of the bone which are cut off from their blood supply die in consequence; and this necrosed bone, upon its subsequent separation, is called a *sequestrum*. Next in frequency to the cortical sequestrum is the central sequestrum—that composed of the bone surrounding the main medullary canal. In extreme cases the whole thickness of the bone, or even the whole bone, may die. This separation of living from dead bone occurs, however, only at a much later period. On an average from three to five months is required for the complete separation in the case of a young adult. The length of this period of time also varies according to the extent of the involvement and the degree of vascularity. In the elderly, the same separation may need, perhaps, as long a period as one year for its accomplishment.

Along the line of demarcation between living and

dead bone, granulations spring up; they start from the blood-vessels. The granulation tissue seems to possess the power to erode and absorb the dead bone with which it is in contact, until at last the sequestrum lies loose upon a bed of granulations springing from the sound bone. In the process of solution of the dead osseous substance, whereby separation is effected, certain salts—such as calcium phosphate—which are not soluble in an alkaline medium, are dissolved and disappear. Hence it is thought that the granulations evolve an acid. Formerly it was believed that lactic acid was the solvent. Tillmanns' later researches seem to show that it is the active, nascent carbonic acid contained in the blood which dissolves the dead bone tissue; and that, in the accomplishment of this, aid is derived from the activities of the osteoclasts.

Unfortunately, this process of absorption is extremely slow, so that we can hardly hope for the complete disappearance of even a moderate-sized sequestrum. Evidences that a certain amount of absorption has already taken place are found, however, upon almost all loose pieces of dead bone.

When a sequestrum lies near the surface of the body, nature is sometimes able to extrude it, and new bone, the *involucrum*, is formed from the granulation tissue, and pushes the sequestrum out. More commonly, however, it cannot escape. The greatest growth of involucrum springs from the periosteum, save in those cases in which the bone-forming layer of the periosteum has been destroyed by the suppurative process; and this new bone of periosteal origin, while it strengthens the shaft as a whole, prevents the escape of the sequestrum. The reason for the failure of a central sequestrum to be ejected is obvious.

For mechanical reasons, therefore, nature cannot, as a rule, complete a cure after separation of the sequestrum. Consequently, if the surgeon does not intervene, there will continue to be, for an indefinite length of time, a discharge of pus through more or less tortuous openings, called *cloacæ*. As regards the kind of intervention which is needed, I will simply state briefly that the surgeon must chisel, saw or drill through the ensheathing involucrum (involving the transverse diameters as little as may be) and release the imprisoned dead bone. It is very unwise to delay interference after the cast-off bone is found to be loose In its cavity, since the patient is thereby subjected to serious danger from exhausting suppuration, from amyloid degeneration of the viscera, from involvement of the neighboring joints in the inflammation, and from hemorrhage, through mechanical erosion of some large nutrient vessel by the jagged sequestrum.

Causation.—Although we have discussed to some extent the pathology of acute suppurative osteomyelitis, we have not as yet dealt with its true cause. The question arises, Have we not here to deal with microbes? Numerous accurate investigations of the pus obtained either directly from the medullary canal or from the depth of the tissues immediately in contact with the bone, and subsequent pure cultivations, have settled this question definitely. "It is not due to a specific poison, however, as was believed to be the case for a long time, but it may be caused by any kind of microorganism which excites acute inflammation and suppuration" (Tillmanns). Among these the variety most frequently found in cases of this nature is *Staphylococcus pyogenes aureus;* less often *Staphylococcus albus* and *Staphylococcus citreus;* and rarely the pneumococcus, the *Bacillus coli*, Eberth's bacillus, the typhoid bacillus, the *Bacillus pyogenes fœtidus* and *pyocyaneus* and the micrococcus pyogenes tenuis and tetragenus, and the streptococci. Although I mention the pyogenic streptococci last, they are far from being the least in importance. They are found chiefly in the osteomyelitis of young children, and this type of the infection is very apt to prove promptly fatal from sepsis.

How are we to explain the entrance of germs into the bone without an apparent traumatism as a doorway? The only plausible assumption seems to be that they pass into the blood through slight abrasions of the mucous or other tegumentary surfaces of the body and eventually find lodgment in the bone. Clinical facts support the theory that, preceding osteomyelitis, patients will be found to have suffered from bronchitis, enteritis, etc. (Kocher).

The majority of cases of this disease, with the exception of suppurative myelitis in connection with compound fracture, occur during the time of the development of the skeleton—*i.e.* during childhood and adolescence. One is inclined to think that the physiological growth of the bone predisposes to inflammatory processes. This theory finds support in the fact that in most cases of acute and chronic myelitis the disease is found to be near the epiphyseal cartilage, and therefore in the most newly formed bone. It furthermore seems to appear with greatest frequency in that end of a long bone which furnishes the greatest amount of growth, and in which the current of blood is least active. It is commonest in the upper end of the tibia and the lower end of the femur; and in the upper end of the humerus and the lower end of the radius and ulna. It will be remembered that the nutrient arteries of the long bones of the lower extremity run *away* from the knee; and in the upper extremity they run *toward* the elbow. A simple way of helping to remember these facts of such practical bearing is as follows: Seated, if one flexes every member sharply upon the trunk—even the first row of knuckles uppermost—then every nutrient artery runs toward the ground.

The selection of the youngest bone tissue as the favorite nidus of the microbes seems dependent unon the peculiar form of the developing blood-vessels. It will be found upon investigation that the sprouting blood-vessels of the growing long bone correspond to wide, hollow spaces close to the epiphyseal cartilage. It will be easily seen that the blood current grows less rapid in these lacunæ, where the capillaries enlarge, thus giving the cocci contained in the blood a better opportunity to precipitate and remain. It is further stated (Hoyer, Rindfleisch) that the blood of the medullary canals flows unenclosed by any tunic in these spaces, and thereby the cocci are brought into direct contact with the bone.

Schiller has demonstrated by a series of experiments that coloring matter introduced into the circulation is retarded in its course and deposited in the blood-vessels of the youngest bone tissue; thus showing, as Heuter says, that there is a tendency for the cocci contained in the blood to be left at this point as a sediment. This being so, we can readily understand how the infection of the young medullary substance occurs.

Clinical Picture.—Sometimes exposure to cold, a wrench or a blow, exhaustion from eruptive fevers, etc., may act as predisposing causes, determining either the time or the seat of the attack, or both. Or, again, no cause whatever may be discoverable. In any case of acute, suppurative osteomyelitis the actual and exciting cause is doubtless always bacterial.

The disease usually begins with one or more chills, followed by fever, which is often very high. In a child delirium is common, and the little sufferer may not be able to point out the seat of pain, which, however, rapidly becomes severe.

With the intensity and mode of infection, and the degree of vital resistance possessed by the patient, the symptoms vary. He may even die within a day or two, overwhelmed by the poison. To rather less severe cases, from a resemblance in the violence of their onset and symptoms, Chassaignac has given the title "typhus des membres." Later, and in more insidious cases, typhoid fever may be simulated. There may be some slight resemblance to a cellular erysipelas. In not a few instances, owing to the fact that the constitutional manifestations alone were taken into account, a dozen other diagnoses—some of them quite absurd—have been made.

Repeated rigors and pyemic temperatures may point to the involvement of more than one bone, or to additional foci in the same bone, or to suppurating foci elsewhere; and pyemia, septicemia, ulcerative endocarditis, etc., may develop in the worst cases, especially in the absence of prompt surgical intervention.

Diagnosis.—The disease with which that under consideration is most often confounded is acute articular rheumatism, and this mistake is especially likely to occur when more than one long bone is attacked. The local symptoms, however, will soon clear up the diagnosis, unless, owing to delirium of the patient, or to the fact that he is too young for speech, attention is not called to the real seat of suffering. Rather near the articular end of the bone, as a rule, a distinct swelling is soon observed. This is caused first by the great congestion and edema of the periosteum and adjacent tissues, and later by the separation of the periosteum from the bone by inflammatory products. While the tenderness over this swelling is very marked, it does not extend beyond the limits of the tumor. Furthermore, unlike what is observed in acute rheumatism, motion of the neighboring joint is not specially painful. The skin over the swelling is not reddened at this time; it may even be paler than normal. Later, when the pus is about to escape through some disintegrating point of its dense sheath, the skin becomes reddened, softened, and gives away.

Treatment.—In the management of a case of acute osteomyelitis in its incipient stages, it must be borne in mind that the inflammation, in a case of this nature, has already produced, or is soon to produce, pus, and that this pus is confined beneath dense, unyielding tissues. The indication is therefore plain; the knife must be used, and that too with as little delay as possible. A free cut should be made through the periosteum, clear down to the bone; and with a dressing forceps entered closed and withdrawn opened, the wound should be enlarged for free drainage. Then it should be irrigated with some antiseptic solution—bichloride of mercury 1 to 2,000, for example—and, if the incision has been made through deep tissues, a drainage tube is to be inserted down to the bone. Otherwise the wound may be packed loosely with wet antiseptic absorbent gauze.

When, in 1854, Chassaignac and other French surgeons advocated a similar free incision, their advice was followed by disastrous results; generally by pyemia and death. That was before the days of antisepsis. To-day, any surgeon who knows what surgical cleanliness means can make such an incision without threatening the life of his patient; and it is, in fact, his duty to employ the knife. Whether this incision alone will be of much value will depend upon whether the infective nidus was situated in the periosteum, or whether that membrane was only secondarily involved by extension of inflammation from the marrow. The latter supposition is in most cases the correct one, and may be considered almost a certainty if drops of free oil be observed between the periosteum and the bone—it evidently having been forced out by the tremendous pressure within the bone.

It is well to wait a very few hours after cutting down to the bone, rather than to penetrate at once to the marrow; unless indeed the violence of the onset seems to the operator disproportionate to the amount of trouble thus far discovered, in which case delay would add to the peril. If, at the end of this period of delay, the local and general symptoms seem aggravated, or at least not diminished in intensity, showing that the trouble is within the bone, and not mainly periosteal, then the trephine should be used, or the burr or chisel, and the marrow should be exposed and treated as follows:

The effective handling of cases of osteomyelitis of the long bones, whether acute, subacute or chronic, has heretofore left much to be wished for. When the infection is caused by streptococci mainly, or other microbes, only less deadly, it is no overstatement to assert that, if treated according to standard methods the result is in perhaps eighty to ninety per cent. of the cases ultimately fatal. This fatality is due almost wholly, in our judgment, to a lack of the extreme thoroughness necessary in dealing with the infected marrow. Once involved at all, to a degree causing symptoms requiring surgical intervention, it is involved usually from end to end. Its softness and great vascularity render such advance on the part of the disease comparatively unopposed, as a rule. To be sure, the *visible* alterations in the nature of the marrow resultant from microbic invasion—the congestion, the mottling, etc.—may and often do extend in recent cases but a short distance up or down from the point of main attack; nevertheless it is the usual and often fatal blunder to cease curetting when the operator has reached apparently normal medullary tissue. He should, if he operates upon such a patient at all, never be contented until he has removed every particle of marrow, from end to end.

The question will at once arise in the mind of the reader: "Is this safe advice? Is it conservative? May the shaft not die if thus deprived of blood-vessels entering the bony Haversian systems from within the canal?" That which conserves life is conservative in the true sense. In all we do, as surgeons, we have to select the lesser evil; and here the risk to the vitality of the bone, from the radical step advised is but little, whereas the risk to life if it is omitted is grave indeed.

There are three ways whereby the long bones receive their nourishment: (*a*) By blood-vessels entering continually from the periosteum, (*b*) through the nutrient arteries, and (*c*) from the endosteum vessels, passing into the bone from its marrow. Of these, if the first two ways be intact, the third way is practically negligible. Or, at least the risk is small indeed in contrast with the enormous advantage obtained by thorough removal of the microbic source of peril.

But this is only one step—and not the first—of several necessary to the proper handling of such cases, according to the method which the writer has found so reliable in his service at the City Hospital, N. Y., and elsewhere; though as yet the number is admittedly but few, and only time can serve to convince the doubting. Ordinarily we should speak far less positively in the presence of small statistics. But even ten or eleven cases of really ugly osteomyelitis recovering with ease and safety, when contrasted with what thirty-two years of experience teach him would have otherwise been the sad fate of most of these patients, would seem to justify a firm stand herein.

Our first operative step is to enter, by chiseling, the shaft at the two extreme ends of its marrow canal—and this, whether or not there may be a compound fracture which gave microbic admittance at some other point along the canal. Drainage with extreme thoroughness is the prime essential here; and we must see to it that we never leave even an inch or so of marrow extending beyond our chisel opening, to make a badly drained pocket at one or other end.

Let us take the femur for example, as that chances to be the bone upon which first we turned what was a rapidly succumbing case into a cure. By testing upon the cadaver it will be found that the upper end of the marrow canal is opposite the base of the lesser trochanter; the lower end opposite a point two to two and one-half centimeters above the adductor magnus tubercle. We enter the bone, after exposing it upon its outer side above, and its inner side below, by aid of chiselling. The opening into the canal should be its full width.

Next comes the radical removal of its marrow; and the question at once arises whether to use sharp or

blunt curettage. By all means do *not* employ a sharp curette. The long Volkmann spoon, for example, by making innumerable fresh wounds upon the endosteum would invite septic absorption. Instead the writer employs what he has termed "pistonage."

A gauze sponge of proper size is firmly rolled up so as to make a piston of such a diameter that it can be with moderate ease drawn again and again, up and down, the length of the canal—the marrow coming freely forth at the two openings. This piston is held rolled in shape by a stout line, like fishline, which is looped around it at about four equal intervals; and the line should extend for convenience a couple of feet beyond either end of the piston. (Fig. 849.) To introduce this instrument we must first pass through the marrow, in at one end and out at the other, a stout soft wire, such as silver or copper, with a tiny loop at one end—the end first introduced—to avoid its piercing the endosteum. Once through the canal and out,

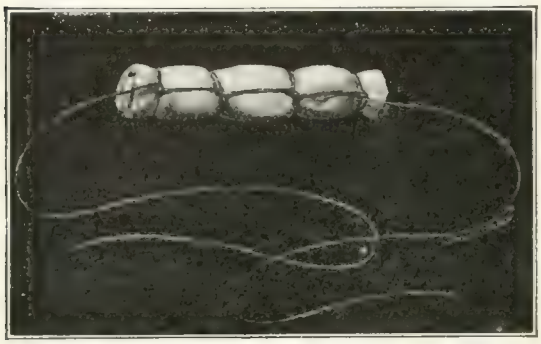

Fig. 849.—Gauze Piston for Cleaning Out the Central Canal in Osteomyelitis.

the fishline is attached to the wire loop, and the wire is withdrawn, bringing the line with it. Now it is a simple matter, if the bony entrance to the canal is chiseled smooth and a little beveled, to introduce by traction the piston, and proceed to clear away all marrow, whether obviously diseased or apparently sound.

The piston may well be wet, before its final removal, with official, seven per cent., tincture of iodine, and by pistonage, this is spread over the lining of the canal.

If bleeding continues to annoy, which has not been the case save in one instance thus far, it is controlled by a piston charged with tincture of iodine; or stopping the lower opening with a firmly-held plug made of a rubber glove or of cotton batting, and by a glass syringe filling the canal with water brought actually boiling to the table-side.

This method we have employed elsewhere in the body in very many cases, as a final step of the "sequestration anemia" operation. (*Annals of Surgery*, February, 1907.) The nearer the temperature is to 212° F., the safer it is, for then almost instantly the tissues so treated turn pale, and blood clots in the vessel-mouths. At a lower temperature (which is inevitable in places high above the sea-level except when the water is heated under pressure) this takes longer to accomplish, with comparative risk of "cooking" the flesh. When properly used, and for but a few seconds, no harm is done even to delicate tissues—such as the deep jugular vein of a child less than one year of age, as the writer personally knows.

To resume the technique: Upon removal of the plug from the lower bony opening, a mass of gauze should be so placed as rapidly to absorb the hot water without having allowed any of it to come into contact with the cuticle.

Finally, the empty canal is now to be filled with sterile paste according to Emil Beck's original and main formula, first cooling it until it is below 120° F. This contains thirty per cent. bismuth subnitrate, sixty per cent. yellow vaseline, five per cent. soft white paraffin, five per cent. white beeswax. This we would modify by substituting the subcarbonate for the subnitrate of bismuth, the latter having in a few instances caused nitrite poisoning. There is no danger of arsenic poisoning, we are assured, nowadays, by competent chemists, in usung the bismuth salts in such full dosage, as it is always carefully eliminated.

In cases where any discharge of a purulent character appears, in spite of our thoroughness, it cannot be severe at worst, and the reheated Beck's paste should be injected again and again at intervals of a few days.

Commonly the bismuth, when the case acts normally, in sinuses is absorbed within three months, and its place is taken by new connective tissue. This process is, of course, much slower within the bony canal.

This same plan, in essence, we have also used in the following bone case, with entire satisfaction; it represents prevention of septic osteomyelitis instead of its cure:

An elderly man was admitted to our hospital service with such an extreme degree of septic involvement of the limb below the knee as demanded prompt amputation. It was not possible to get flaps permitting a knee disarticulation, which for obvious reasons would have been preferable; instead, the femur had to be sawn across about three to four centimeters above the lower end of the marrow canal. As all know, the periosteum of this long bone is so thin as to be almost wholly valueless as a cuff to cover the marrow-end and prevent a septic osteomyelitis. This we knew to be inevitable by ordinary methods, since the skin constituting our flaps had for months been full of infective material, its lymphatic vessels having, of course, conveyed the microbic trouble from the almost rotten leg below. It was therefore a certainty that the stump must suppurate; however, we hoped to prevent the otherwise sure extension up the open marrow canal. This was done by the method just described—with these modifications. It was most essential not to prolong the duration of the operation lest we lose the weakened patient from this reason. Therefore we did not chisel into the upper end of the marrow canal—neither did we use (in this single case) the gauze piston. Instead we simply cleared out all the marrow with a very long Volkmann spoon-irrigator, which flushed out at the same time. As the marrow was not infected we did not fear to use the sharp spoon. Next, the empty canal was dried out with small pledgets on a long applicator, and swabbed with tincture of iodine; and finally was filled even full with Beck's paste. Obviously, this plan added but a very few minutes to the operation—and the resulting safeguard to the patient was so plain a one that I think nobody will gainsay it. The result justified our expectations. The pus appeared within the flaps, of course, and was drained away thoroughly by tubes for the purpose; but the final result was recovery and a useful stump, and with no bony involvement whatever.

The constitutional treatment consists simply of measures intended to support the patient's strength. It is, perhaps, of little avail to give antiseptics; still, the safer ones—as benzoate or salicylate of soda—may be employed. It may also be well to use free inunctions of the Credé liquid silver ointment. The writer's experience, as stated in the second edition of this work was then adverse to the employment of sera and antitoxins. To-day, however, our first step *post-operationem* should be to ascertain the exact nature of our microbic enemies by examining the pus or the diseased marrow, also which ones are relatively

the more preponderant. Then without an hour's needless delay, we should give by hypodermic an appropriate serum injection, repeating it in a few days, or p.r.n. The effects of this, prepared by skilled bacteriologists are often of striking benefit. But when used "shotgun-prescription-wise" and without accurate knowledge first obtained by the surgeon, as stated above, such injections may well do much more harm than good.

As regards those cases which are seen at a later stage and in which the disease is complicated by the presence of a certain extent of necrosis of the bone tissue, the practical questions which present themselves are these: How is the existence of such a bone necrosis to be ascertained? and, What steps are to be taken for the relief of the condition after we have discovered its existence? By the intelligent use of the flexible silver probe—or, in certain cases, of two probes—the surgeon should have no difficulty in ascertaining that a necrosis exists, and also occasionally in determining how great is its extent, and whether the necrosed portion is or is not loose. In other instances, however, he will be forced to resort to an explorative operation in order to determine to how great an extent the bone is necrosed, and whether the sequestrum has become sufficiently detached to warrant the adoption of radical surgical measures for the removal of the dead bone. Furthermore, in reaching the latter decision he will have to weigh very carefully the question how far the patient's health is being undermined by the constant discharge of pus which invariably accompanies the separation of the dead from the living bone.

The late Prof. Thomas M. Markoe, in his article on "Necrosis" in the first edition of the Handbook, expressed himself as follows in regard to the steps which should be taken in the presence of a necrosed condition of the bone:

"Having now settled the question as to the propriety of operation, the time of its performance may be considered. As a general rule, it is better to remove the sequestrum just as soon as it can be ascertained to be loose. But if the patient be much reduced in health, if the season be unfavorable, and if the discharges and the sufferings from the local disease be not excessive or exhausting, then it is quite proper, and generally quite safe, to wait until, by careful attention to nutrition, by fresh air and exercise, perhaps by change of air and surroundings, we secure a better reparative condition of the system, in view of the often serious operation which is contemplated. If there be no considerations of this nature, the operation should be undertaken without unnecessary delay.

"The operation itself consists in releasing the sequestrum from its mechanical confinement within the tissues, and removing it. The operative procedure will vary, therefore, with the extent and solidity of the tissues enclosing the sequestrum, and with the accessibility of the sequestrum from the surface. In most cases of superficial necrosis, or exfoliation, it is only necessary to divide the soft parts covering the dead piece in order to remove it with great ease. This, however, is not always the case in exfoliation, for it sometimes happens that the dead plate extends on the sides of the bone far from the surface, and it occasionally occurs that a thin plate of superficial necrosis surrounds completely certain portions of the shaft of the bone, thus producing a condition of things which renders operation extremely tedious and severe, and, not infrequently, even then the entire removal of the deepest portions of the sequestrum is not accomplished.

"To take a typical case of necrosis of the shaft of the tibia, where the diagnosis is clear, the involucrum sufficient, and the sequestrum entirely separated, the steps of the operation may be described as follows: A free incision is made on the anterior surface of the limb, where the bone is most superficial, and this incision should extend as far as the supposed limits of the necrotic action, and may be crossed by another at about its middle, so as to give easy access to the surface of the involucrum. The flap then being dissected up clean from the exposed bony surface, we select the most favorable point for attacking the bone case enclosing the sequestrum. This is generally to be found at one of the larger cloacæ, which, being further enlarged by the chisel or gouge, soon gives us access to the cavity in which the dead bone lies. By means of this first exposure of the cavity we learn the size, the degree of freedom, and the extent of the sequestrum, and we take our measures accordingly. If the sequestrum prove to be very long, then the incision through the involucrum must be extended so as, if possible, to release it without breaking off any of the irregular and slender processes in which it terminates. About this the operator should be extremely careful, as, if any of these fragments are left in the bottom of the wound, they are apt to give trouble, and if we cannot reach and remove them with slender forceps they are frequently a long time in making their way to the surface, during which time, of course, the wound will not heal. In exposing one of these large sequestra, it should be borne in mind that restoration of the involucral bone which we are cutting away takes place to only a very limited extent, particularly in those who have passed the earlier periods of life. It must be remembered that nature has already, in forming the involcrum, accomplished a very elaborate and extensive restoration of bone, and if we destroy this new formation she will hesitate about repeating the process. In point of fact, we find that the cavity left after these operations does not, except in very young subjects, fill up with bone, but rather with a firm, fibrous, cicatricial tissue, which, while it fills up the gap left in the bone, contributes very little to its strength. We must be careful, therefore, not to weaken the bone by any unnecessary cutting in its transverse diameter, though in the longitudinal direction we may proceed with more freedom. The cutting is done most satisfactorily, I think, with a gouge, though if a cloaca is not in a favorable position for enlargement a small trephine answers a good purpose in making the first opening through the involucrum. The gouge and the rongeur, however, will be all that in most instances will be required. After the removal of the sequestrum a careful examination should be made with the finger and the probe, to make sure that no fragments remain, and that no cavities are left without sufficient openings to secure drainage."

By way of supplementing the remarks quoted above I will state that it is important, after laying bare the bone, to curette away the entire granulating surface, and to sterilize the living bone, thus laid bare, by peroxide of hydrogen or other effective means. Often such curetting lays bare the entrance to more than one chamber containing sequestra. There may even be a chain of such running along the marrow. And unless the operator makes sure by probe and curette that this is not the case, his work, in removing the first sequestrum exposed, may prove by no means a success; and a continuing discharge of pus will show that he has not removed the whole cause. Following these steps, it is possible by many ways to treat the bony cavity in an endeavor to hasten its healing. For a study of these, see *Bone, Plastic Surgery of.*

Acute Epiphysitis.—Acute epiphysitis presents problems of the gravest importance. In addition to the risk of a suppurative joint trouble, by extension, the focus of infection—whether it begins in the shaft or in the epiphysis—is commonly close to the narrow line of cartilage which connects the two. The importance of this lies in the fact that if the cartilage

become severely involved in the inflammation there may result a diastasis—*i.e.* a separation of the epiphysis from the shaft, with dislocation, a condition which demands the utmost care and the most skilful splinting to prevent a final deformity from union in a bad position. Even when the involvement of the cartilage is somewhat less grave, if the normal cellular activity in the vicinity of this narrow line of cartilage be permanently impaired or destroyed, growth of the bone, so far as this end is concerned, will cease. And the seriousness of this circumstances is still further enhanced by the fact that the greater portion of the growth of the long bones takes place normally from that end which is most subject to attacks of acute osteitis. For example, in the case of the long bones of the extremities the ends which are nearest the knee, and farthest from the elbow, supply most of the growth, and are also more subject to acute osteitis than are the opposite ends. And—to mention a single instance only—von Bruns has collected evidence which shows that diastasis of the femur from all causes occurs in the proportion of twenty-eight cases of separation of the lower epiphysis to one of the upper. And according to Ollier, the development in length of the thigh bone is about two-thirds from the epiphyseal cartilage of the lower end and one-third from that of the upper end. When it occurs in a little child, a diastasis of the lower end of the femur, even though the separated parts are properly replaced, and adequately splinted until bony union shall have taken place, may result in a shortening of as much as nine inches; whereas if the diastasis occurs at the upper end, the records show that only about half this amount of final deformity results. These are facts, therefore, which it behooves the physician in charge to know in order that he may, for his own protection, and especially in view of the possibility of a suit for malpractice, give timely warning to the parents.

Treatment.—As regards the treatment of acute epiphysitis, prompt surgical intervention and careful splinting to prevent diastasis are the only means worth mentioning. On the other hand, the proper management of the sequelæ will depend upon the precise character of the pathological conditions left by the acute disease. A problem very difficult to solve is that which is presented when the epiphyseal cartilage of only one of the two bones (of either the forearm or the leg) is involved by the disease. In such a case growth will be entirely arrested in one bone while it will continue to take place in the other. Under such conditions the ultimate result—if the parts are left to themselves—can scarcely fail to be a dwarfed and grotesquely twisted limb. Surgical intervention may be resorted to at a relatively early period, with the idea of preventing the evil to which attention has just been called, or surgical measures may be adopted for the correction of the deformity after it has been fully established.

In the former case the surgeon, having to do with a case of diastasis, should—after all suppuration has ceased —chisel through the thin plane of cartilage of the neighboring or sound bone of the same extremity. This stops the growth of that bone, and results in a straight though shortened limb. On the other hand, if interference is postponed until the deformity shall have reached its full measure of development, the surgeon will have to tax his ingenuity by the employment of various means (chiseling, aseptic fracturing, resection, etc.), to overcome in a measure the extreme deformity so commonly found at that time. The brightest suggestion as to a measure of *prevention* here is that of Murphy of Chicago—though as yet it has never been tried out. This is to chisel or saw away that condyle or that end of the bone whose epiphyseal cartilage has been destroyed, and insert a bone-graft in its place containing a similar line of cartilage either from the bone of another child, or from some growing animal of slow growth.

Chronic Osteomyelitis.—There are certain cases of subacute and chronic osteomyelitis, limited in extent and indicating a mild degree of bone infection, which deserve mention. They are accompanied by more or less pain and tenderness of the bone over a small area, and this may continue for months and years with slight or no constitutional symptoms. In some of these cases called "Brodie's abscess," the pus may finally reach the surface, or may remain permanently surrounded by compact bone; an osteoporosis has occurred, sufficiently great to hollow out a pus cavity, usually lined with granulations; but commonly no necrosis—no death *en masse*—takes place. It may be that a few of these abscesses represent the site of softened and broken-down gummata of late syphilis.

The treatment is self-evident. By means of the trephine the cavity is to be reached and drained. Even supposing the diagnosis to be erroneous; supposing the case to be in reality that uncommon disease, a neuralgic osteitis—one in which a chronically congested vascular state in the bone seems to induce nerve dystrophia and consequent neuralgia—experience proves that penetration of the bone gives the surest relief, and is a safe operation.

Rheumatic Osteitis does occur, but is very infrequent, and is apt to be secondary to rheumatic periostitis. The coexistence of rheumatism elsewhere in the fibrous framework aids the diagnosis. Heat, counterirritation, and, as a last resource, opening the bone, give the greatest relief, and should be conjoined with the usual purely medicinal and hygienic means of treatment.

Syphilitic Osteitis presents itself chiefly as a result of gummatous involvement in the later stages of the disease. It is also, however, to be noted as one of the manifestations of inherited syphilis. The osteochondritis of infants, first described by Wegner, is a frequent manifestation, as is also dactylitis syphilitica. Regarding the former, Taylor states that it is often the only sign of this inheritance; and that at other times its presence decides the syphilitic nature of coexisting lesions. It involves chiefly the shafts and epiphyseal junctions of the long bones; and is usually found at birth or within the following month. The swellings are rather distinctly limited, as a rule, and the babies suffer when they are handled. In bad cases separation of the epiphyses, suppurative osteomyelitis, and necrosis may develop.

The dactylitis when present affects mainly the first phalanges. It differs from the tuberculous variety in this regard, as also in the fact that when luetic it is apt to be multiple, and to appear upon both hands.

"Parrot's nodes," involving the two halves of the frontal bone and the two parietal bones are found in infancy, and are due to the same cause. These swellings, upon all sides of the anterior fontanel, are very characteristic, and are caused by both a periostitis and an osteitis of these bones.

In later childhood and in adolescence are found the bony irregularities, hypertrophies, and asymmetries which often are so characteristic of syphilis. In the face, the nasal bones are those which suffer most. As a result of necrosis of the bony support the nose undergoes shortening, the lower part retreating toward the upper part; or else the bridge is sunken. Of the remaining parts of the skeleton the tibia presents the most striking of these late bony inflammatory changes due to syphilis. It may be greatly thickened, its crest being no longer a mere ridge, but broadened and swelling forward, so that when seen from one side the tibia presents the characteristic shape of a saber.

For a fuller study of the bony stigmata of this disease, including the pathology and clinical course of gumma of bone, the reader is referred to the article upon *Syphilis*.

Necrosis of the Jaws Dependent upon the Action of Phosphorus.—This is caused by the fumes of the ordinary yellow phosphorus. Now, by legislative enactment, almost everywhere in match-factories the red or allotropic form of phosphorus has replaced it—with infinite benefit to the workers in these factories. This is a condition which the surgeons of the present generation rarely have the opportunity of observing. I may therefore be permitted again to quote from Professor Markoe's article on "Necrosis" in the first edition of this work.

"These cases occur almost exclusively among the operatives in match factories, who are living in an atmosphere containing the fumes of phosphorus and phosphorous acid. The workmen most liable to be affected are those employed in the dipping-room, and in the packing-rooms. In the first there is a constant prevalence of the fumes of the volatilized phosphorus, and the air in the second is still further vitiated by phosphorous acid from the frequent burning of the matches while being counted and packed. It is believed that these phosphorous emanations, which are quite soluble in water, are dissolved in the saliva, and thus come in contact with the teeth and gums, upon which latter the poison seems to exert its primary influence. Why these particular parts are selected by the poison in preference to the rest of the buccal and to the Schneiderian membrane, which are equally, if not more, exposed to its action, is a pathological fact which we are not able to explain. That the poisonous action is a local, not a general, one seems further proved by the fact that constitutional cachexia does not often appear as a condition preceding the local outbreak; and still more strongly by the fact that if the teeth be sound, and the gums unbroken, the disease is rarely developed. On the other hand, it ought to be stated that there are sometimes evidences of slow systemic poisoning by phosphorus, terminating in necrosis; and also that it is rarely those who have been for only a short period subjected to the poison who develop necrosis, but rather those who have been some years in the occupation. Again, it has been recorded that the prolonged internal use of phosphorus may lead to typical necrosis of the jaw, as in a case recently reported by Mr. Hutchinson. It may, therefore, in the light of our present knowledge, be assumed that the action of the poison, at least in most cases, is purely a local one, though the system is probably predisposed to the local outbreak by a constitutional infection from the poison slowly introduced into the blood, either by inhalation of the vapor or by the ingestion of the drug as a medicine. It acts by inflaming first the gums and the linings of the tooth sockets, from these spreading to the alveolar processes of the bone, and finally, by extension by continuity, involving a large part, and not infrequently the whole, of the bone. This destruction of the entire bone is sometimes found in the lower jaw. In all the cases I have seen affecting the upper jaw, the ravages of the disease were mainly confined to the alveolar arch."

Osteitis Deformans.—This essentially chronic condition is, though recognized and studied since 1876, still illy understood as to its etiology. It occurs most often in middle age, and involves perhaps more frequently the long bones, but also at times the skull, pelvis, and vertebræ. Hypertrophy may go hand-in-hand with softening, resulting in malformations which give the disease its name. Nevertheless, it does not advance to the extent of causing fractures. Some authors—Tillmanns for instance—differentiate two clinical varieties, the painful and the painless. The former is the more frequent, usually involving the bones of the lower limbs. The painless is believed to occur more often in the upper limbs, and in females rather than in males. Generally several bones are involved, thus indicating a systemic rather than a local cause. Treatment has thus far proved of little avail; and since we cannot definitely ascertain the real cause and direct our treatment to that, the only course which remains to us is to alleviate pain or other symptoms.

Tuberculous Osteitis.—Under this title we shall discuss that inflammation of bone which, until within a few years, writers have studied under the name of caries; paying more attention, as in necrosis, to the result of the process than to the causative agent. Nevertheless we should mention the fact that now four varieties of the tubercle bacillus are recognized: (1) That chiefly causing human tuberculosis; (2) the bovine, causing tuberculosis in cattle, chiefly; (3) the avian, affecting birds; and (4) the reptilian, as found in turtles, etc., for instance.

Tuberculous involvement of bone is in a large majority of the cases caused by the activities of the human type of bacillus; in a smaller number by the bovine. The others are negligible as factors.

Thus, the Royal Commission of Great Britain, out of sixty cases of tuberculosis elsewhere than in bone, in man, found fourteen bovine and forty of human type. As to bony involvement this Commission has decided that it is due to the human bacilli; and that, therefore, attainment of a perfectly pure milk-supply will not prevent its development.

This is a chronic malady, affecting mainly the red-marrowed, cancellous bones, such as the bodies of the vertebræ and the carpal and tarsal bones. It is essentially an osteoporosis, with tuberculous deposit as its cause and accompaniment, and it results in molecular death of the bone. Sometimes, by extension, the compact tissues are involved, but here the bone first changes its character, becoming cancellous through osteoporosis; and later even the remaining bone trabeculæ may disintegrate, and a suppurating cavity be left. The lime salts are dissolved, and the remaining membranous or gelatinous bone breaks down under the devitalizing influence of the tubercles.

It may be objected to the term *tuberculous* that caries is not always of this nature. It is undoubtedly true, however, that chronic, granulating, rarefying osteitis is commonly so, and at the present day the cases of caries in which careful investigation fails to find the bacillus tuberculosis are very few, and are becoming fewer.

The bone frequently expands in one or both of its diameters while becoming a mere shell filled with pus, bony detritus, and granulations. Apparently the growing mass of granulation tissue forces out the walls of bone when they become thin enough to permit it. A rather common example of this condition is found in "spina ventosa." Here the bone—a metacarpal, for instance—may gradually assume the shape of a spindle. Syphilitic dactylitis may produce the same distention; this latter inflammation, which is usually a result of inherited syphilis, most often involves one of the first phalanges.

The deposit of tuberculous material in bone may or may not present all the ordinary appearances of a focus of tuberculous disease. It may undergo caseation, or it may, as it usually does, soften and liquefy. Some suppuration is probably always present, but this varies greatly in degree. In the caries of children it is almost always a feature. Pott's disease, for example, is accompanied by the formation of so-called "cold abscesses" of varying size, and the pus starting from the disintegrating bone follows a downward course, governed by gravity and the path of least resistance, and may finally find an exit for itself upon the surface. Or, in cases with less discharge, the pus may become cheesy, its ensheathing connective-tissue covering may undergo a change into calcareous material, and the abscess may never descend far from the diseased vertebral bodies which gave it origin. Such an abscess may be discovered only at the autopsy.

In elderly individuals the formation of granulation

tissue and a slow advance of the disease, with but slight discharge—a "caries sicca"—are generally to be expected.

Tuberculous osteitis may occur at any age, but it develops more commonly in early childhood than at any other time. From five to fifteen years of age is the time of its greatest prevalence. Its onset is usually insidious. The patient may, after a time, complain of a little tenderness or aching after exertion. Later, some swelling of the bone may perhaps be noted. The skin is not involved at first; after several weeks—possibly months—it becomes distended, looks inflamed, breaks down at one or several points, and gives exit to pus. This pus varies in consistency, and is sometimes gritty to the feel, containing minute spicula of bone. A probe introduced may—if the sinus be moderately straight—touch bare bone, and may by moderate pressure be made to fix itself firmly in the cancellous tissue; this could not be done in the case of the compact sequestrum of necrosis. The lips of the sinuses and their walls soon become lined with flabby, inactive granulations, in which the bacilli are sometimes to be discovered. Meanwhile the patient may be subject to more or less fever, night sweats, and similar signs of vital depression.

By extension a caries may involve an adjacent joint, with resulting "white swelling" and all the manifestations of tuberculous osteoarthritis. Or, conversely, a primary joint tuberculosis may lead to erosion of the articular lamella of the bone, and then to tuberculosis of the cancellous tissue.

Caries commonly, though not invariably, makes its appearance in individuals of the so-called scrofulous diathesis—*i.e.* those who are especially subject to affections of the glands, skin, and mucous surfaces. Often a family history of tuberculosis may be obtained, or it may be learned that the parents died from some unnamed lung trouble. The patient is apt to be pale and anemic in appearance although this is not always the case. In adults the bone disease is sometimes a reappearance of inflammation which existed there for a time during childhood, and then remained for years quiescent.

At any stage in its progress the disease may come to an end, and reparative processes of varying degree begin. Caries does not necessarily go on to the complete destruction of all the cancellous bone involved. If the patient's general condition can be improved, so that the vitality of the bone is enabled to resist the encroachment of the tuberculous disease, suppuration may cease, fistulous sinuses close, and new bone form to some extent. This is the rule in Pott's disease. The bodies of one, two, or sometimes more vertebræ melt away, the comparatively sound bodies above and below come in contact, and if the patient continues to live, as he commonly does, the disease is brought to an end, and the vertebral bodies near the focus of the disease, but which have escaped, unite by firm bony union. In some bones—the calcaneum for example—there is very little tendency to bony repair. The space once occupied by bone becomes partly filled by simple connective tissue.

It is important to bear in mind that a mere local bone-tuberculosis may at any time give rise to a general tuberculosis. Although such a catastrophe is quite exceptional, it does sometimes occur. Therefore, when it is possible to remove by surgical means the diseased bone, it should be done. It has even been suggested, of late, that in spinal caries an attempt be made to scoop away the diseased tissue and thus hasten recovery; if need be, resecting one or more ribs to allow thorough work. But whether this becomes a recognized practice or not, in all readily accessible regions the proper treatment consists in the free use of Volkmann's sharp spoon; the most thorough work under these circumstances being always the best. As with suppurating tuberculous lymph nodes so here this treatment may save months of effort on the part of nature to remove the tuberculous deposit.

It goes without saying that surgical cleanliness must be strictly observed during and after the operation.

It is to be expected that, in many instances, one such scraping will not suffice entirely to put a stop to the disease. Perhaps the step may have to be repeated a number of times before all the affected tissue is reached and eliminated. During the dressing of bones or of sinuses which have been operated upon for caries, iodine should be our main reliance. In irrigation we may wisely employ a one- or a two-per-cent. solution of the pharmacopœial tincture, which does not precipitate, and is seven per cent. iodine. This strength will stain the tissues a yellowish hue.

The gauze used for packing and drainage should be first moistened, and then well rubbed with some one of the numerous powders which depend for their value chiefly upon the iodine which they contain—such as (in order of strength) iodoform, iodol, nosophen, aristol, and europhen. The author rather inclines to aristol, and considers it practically as effective as iodoform without the objectionable odor of the latter.

In obstinate cases of caries, after the vigorous use of the sharp curette or gouge, it is well to cauterize also before beginning the iodine treatment. Perhaps the application first of pure carbolic acid and then of strong alcohol is as effective a measure as any that can be adopted. The severity of this procedure may be easily regulated by shortening or protracting the time during which the pure acid is allowed to remain in contact with the parts before the neutralizing action of the alcohol is brought to bear upon them.

The prognosis in children, after such thorough treatment, is fairly good. In adults it is distinctly more difficult to eradicate the disease completely. In the tarsal bones, for example, it is questionable whether in adults it is not wiser to excise entirely the affected bone or bones in order to prevent a relapse.

When despite thorough local treatment the disease extends and perhaps involves an entire extremity, amputation at some distance above may be our only remaining resource.

Regarding medicinal treatment, cod-liver oil, iron, and good nourishment are to be administered in the hope of improving the general condition. In the phlegmatic temperament cold bathing daily is of more value than the oil. These means, however, will not remove the bacilli from the bone marrow. They are merely useful adjuvants to the proper local treatment.

In conclusion: We have already commented upon the fact that softening, due to a rapid decalcification, is one of the earliest changes resultant from bone tuberculosis. It is equally true that in sarcoma and carcinoma of bone this is the earliest clinical sign. For really hopeful results from operation everything depends upon how early malignancy is recognized; and in several respects tuberculosis of bone may be considered one of the malignant manifestations. It is certainly more apt to recur, especially in the adult, after apparently thorough excision, than is giant-celled sarcoma for one instance, whether *in loco* or at a distance.

In all of these malignant conditions just named, before any other change is clinically manifest—before even any alteration occurs in shape or size of the bone in question, and prior even to the time when the *x*-ray can serve as a guide—softening manifests itself; and this is easily capable of proof.

We should use a stout ordinary sewing-needle—not a surgical needle with a cutting edge. This cannot be made to enter even cancellous bone, if it be normal, without the use of extreme force. In malignancy the difference is plain; the needle enters as if being thrust into cartilage.

Lest it be snapped off and the point left in the bone, due to some sudden, unwary movement of the

patient, we should withdraw the temper a little from the point—enough to turn it steel blue—by passing it a second or two through an alcohol flame. While making the bony test, hold it firmly by a needle-holder. Compare the two sides at exactly identical points, as to degree of resistance to the advance of the needle.

We must of course differentiate from softening due to benign (*i.e.* non-malignant)—osteitis, from rachitis, from osteomalacia, from syphilis, etc. As to the first of these, the thermometer (when acute) with the usual symptoms accompanying inflammation, microbes in evidence, etc., will help us. The next two diseases named involve not one, but several bones. There are also the characteristic constitutional symptoms.

As to syphilis of bone—by this we mean gumma—assuredly here, too, in this semi-malignant condition we have very early softening due to decalcification as the first recognizable step, locally. But almost invariably the history of the case with its several secondary manifestations, and very likely other tertiary ones, will serve for differential diagnosis.

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Bone, Plastic Surgery of.—The principles of successful plastic surgery of the soft parts apply in the main with equal force to plastic surgery of bone. There must be absolute asepsis. The grafts must fit comfortably, for undue pressure would prevent to some degree the passage of even the vitalized plasma of the blood upon which, the vessels being all obstructed by clotting, both tiny bone fragments and greater ones must depend for their nourishment by capillary attraction. Again, absolute immobilization is essential, and for a much longer time than is true with grafts of soft tissue. Just as the healing of fracture is found always to be a painfully, a tediously slow process, nature acting as if she had dateless Olympian leisure in which to do her work, and not even starting her process of callus-exuding to any appreciable degree until an average of ten days has elapsed, so it is with these comminuted fractures for grafting—fragments, largely of the surgeons' making. Once begun, the callus—nature's glue—is steadily poured out for about ten days more before "knitting" starts. In the child this period begins two or three days earlier; in the elderly as much later; but the average is as stated. It varies, too, with the relative vascularity of the bone and flesh in question surrounding our grafts—and in amount, with the degree of vital energy, also upon the perfection of immobilization. Where the grafts—or the bony ends of a fracture—are kept properly quiet, there is little of the waste of energy which the exudation of "provisional" callus implies. The "definitive" alone remains ultimately to become new bone.

The deposit of lime salts in the callus and the migration into it of myriads of bone-cells—in a word, the numerous changes wherein and whereby it ultimately becomes "bone of our bone," require from several weeks to a few months to become reliably firm and solid. For the surgeon's own protection he should explain to the patient, in the beginning, this relative slowness as compared with the healing of plastic work upon the soft parts.

CLASSIFICATION.—The following classification of this subject may simplify our study of it, to some extent:

I. Callus—the material from which bone is made: How to increase it in amount.

II. Autogenous bone-grafts: (*a*) With pedicle, either from the bone to be grafted upon, or from another bone. (*b*) Without pedicle, and supplied either by the patient or by another human being; either in minute fragments or in mass.

III. Heterogenous bone-grafts: taken from the living lower animals; also from those that are dead.

IV. Plastic bone-fillings: (*a*) From the living. (*b*) From other than living sources.

I. CALLUS.—The material of which nature manufactures new bone, deserves first place in our study of this subject. It is fibrin, pure and simple, but with a different destiny from that of a similar lump of nature's glue exuded elsewhere in the body, because of its being here in contact with bone. Among the well-known ways of causing it to appear in large quantities let us mention three:

(*a*) Method of H. O. Thomas, by daily use of a small percussion-hammer, whereby the region of the broken bone—for it was in non-union of fracture only that Thomas used it—becomes tender to the touch, and hot from determination of blood causing active congestion.

(*b*) "Hot Damming" method of Bier of Berlin. In this, by elastic cording upon the proximal side of the fracture or bone-graft, for several hours per day, and during a period of weeks, a greater plastic exudate inevitably occurs—the cording must not be tight enough to cause the limb to become cold, hence, the title.

(*c*) Method of Bier wherein blood is withdrawn from a donor and injected at the point where more fibrin is needed. This is admittedly a means of making use of the fibrin present in the blood so injected, and the other ingredients of it are not of value for this purpose; indeed, unless extreme precaution is taken both as to rigid asepsis and as to a preliminary Wassermann test for syphilis, it may conceivably not be free from danger.

(*d*) A fourth way, the writer's now employed by him for some ten years at least, but only recently published, because he wished enough cases of fracture with non-union and of plastic bone work to make it conclusive. It was described, however, by the writer at the same meetng of the Surgical Section of the American Medical Association in St Paul, Minn., at which Bier, through a younger colleague from Germany, spoke upon his blood-injection plan.

This plan consists simply in the injecting of sterile glycerite of tannin, of ten per cent. strength, by a long spinal needle, between the bone-ends, in non-union, or when in plastic bone work we need material to be moulded into new bone.

It may be not without interest to know how this method was hit upon. A generation ago a peripatetic doctor named Heaton traveled about the country advertising "Rupture cured without the knife." He finally divulged his secret—which was that after reducing the hernia, leaving the sac empty, he injected into this sac as strong a decoction of fresh white oak bark in boiling glycerin as he could make. This caused, during its absorption, so free an exudate that a mass of fibrin filled the sac, preventing the return of the hernia—at least for a while. This method of attempting the cure is a poor one, as has since been proved, for the neck of the sac remains open, and in course of time the hernia again stretches its way out. However, our interest is not as to this, but regarding glycerite of tannin, in its curious property of causing by its presence an exudate which the several pathologists and histologists to whom we have referred the point considered identical with callus—both being simply fibrin, though with a different destiny according to whether thrown out in contact with bone or elsewhere.

Quercus alba, the white oak, contains in its bark no ingredients of the least importance except tannin. This is present to the extent of about ten per cent. Now the official U. S. P. glycerite of tannin is twenty per cent. in strength. By diluting this with an equal amount of glycerin and sterilizing by boiling, we have in effect what Heaton used, but prepared with greater simplicity and scientific accuracy.

It occured to us, when thinking of Heaton's method many years ago, that fibrin thus produced would perhaps prove a most efficient means of supplying callus—and this has proved true; indeed, the most so of any method of which the writer is aware. Although his hospital is a large one he has had but semi-occasional opportunities to try out the plan. Its use in plastic surgery of bone is obviously recent, since this branch of our science is new. And as to fractures, by far the greater number of cases of non-union are not caused by lack of vital power to induce enough callus, but due to lack of proper apposition or to intervening soft tissues, or dead bone-fragments between the ends; reasons that call for operating far more frequently than simply for more callus. However, when used in properly selected cases we are now willing to speak strongly as to the benefits to be expected from glycerite of tannin. The amount to be injected varies according to the case. In non-union of fractured tibia, for example, we inject—after passing the needle through an inch or more of flesh and then between the fragments, perhaps a dram. This is to be repeated after several days, or not, according to the degree of congestion and tenderness resultant. A lump of "provisional callus" can soon be felt.

It is being used to produce a new head for the humerus in the following case now in our service at the City Hospital. A woman of thirty came in with a subglenoid dislocation of two years duration. The operation which seemed best and was duly performed was, after failure to accomplish non-operative reduction, to make a vertical incision near the anterior edge of the deltoid muscle, so as to divide as little of the circumflex nerve as possible. By an aneurysm-needle a stout linen string was passed about the humerus at as high a point as possible. By this a Gigli wire saw was drawn into position and the bone was sawn across—leaving the head and part of the tuberosities behind (to be removed by rongeur, from the axilla, at a later date, if it gives trouble). The glenoid cavity was dissected empty, the capsule closed and sutured, and the elbow put in Velpeau's position so that the pressure of the long axis of the humerus was upon the outer or untorn side of the capsule. Just before closing the capsule a spinal needle with its well-oiled trocar in place was passed vertically down from about the tip of the acromion process so that its point lay free in the glenoid cavity. When ten days had passed, giving time for the capsule-wound to heal, and being then also about the time when nature begins exudation of callus, we helped along this activity by injecting through the long needle about ʒiij. of the glycerite of tannin (modified as above described), thrown directly in contact with the sawn surface of the upper end of the shaft; and the needle was then withdrawn. The arm was not moved, nor will it be until some three weeks further have elapsed; when by active and passive motion we expect to help mould a respectable head—a more or less globular upper end of the humerus. This same thing we have had but two other opportunities to accomplish heretofore, but these were satisfactory.

In another line of bone-plastic work we have repeatedly used this plan, as the letter quoted below instances. This case is selected because of the extreme age of the patient in question, which adds interest to the excellent result. The letter from Dr. W. Hanna Thomson, dated November 15, 1910, and addressed to the present writer, reads as follows: "I wish to record for you my observation of the case of an old lady, eighty-one years of age, who fractured the neck of the femur (intracapsular) by a fall. She was a former patient of mine and on that account wanted my opinion as to the advisability of your proposal to unite the trochanter with the broken head of the femur now loose in the hip-joint. On hearing your description of the operation, the like of which I had never myself seen, of introducing an aluminum nail from the trochanter into the broken segment in the acetabulum, I agreed to it and was present at the operation. It was then discovered, however, that the bony structures involved were so hollowed out by senile changes in them that something else had to be done to afford any support for the weight which would be thrown upon them. You then proposed to inject glycerite of tannin along the track of the nail and into the joint. This was done, and in the course of time the presence of this tannin excited such an exudation of callus material that a firm union took place, with the result that the old lady was able to go up and down two flights of stairs to her meals. I regard this as the most extraordinarily successful procedure in a very difficult surgical complication that I have witnessed; and I congratulate you both for the ingenuity and for the skill with which the operation was performed."

An aluminum spike was used because this metal, by action of the alkaline blood, is in about two years' time dissolved. It is no longer needed, by then; and being a possible source of future trouble if not soluble, we are glad to get rid of it. The finding of the upper end of the femur reduced to a thin outer shell of bone, with a soft, marrow-like material within, is common enough in the old, and is the reason why there is much need of a reliable means of producing a considerable amount of new bone here.

The spinal needle is passed along the course of the nail as a guide, until its point is between the two fragments of the broken femoral neck. There it remains, and a needle of just the right length should be selected so that its base, with the trocar in place, lies just outside the skin. The nail is now driven home—of such a chosen length that its point is against the convexity of the head, and its base in the dense bone of the cortex of the shaft, a little below the great trochanter. It is hollowed at its base to hold the point of a nail-set while being driven in.

The thighs are held widely apart—in extreme abduction (Whitman's position). This must be done to both, and is maintained by a strong plaster-of-Paris splint, going from waist-line to toes. The patient is not to be kept in bed save at night, to avoid risk of hypostatic pneumonia. By about the tenth day the sutured capsule will have healed enough to justify the injection of the glycerite of tannin—a half ounce or more, part of which in a case such as that described in the above letter will of course remain within the hollow neck of the bone. The needle is now withdrawn.

Of course a trap-door has to be cut in the splint to expose the base of the needle for attachment of the syringe thereto.

When about three weeks have elapsed from the date of the operation, the patient in this, and in every other fracture case in our hands, is put upon large doses of lactate of calcium, to hasten deposit of lime salts in the new bone.

II. Autogenous Bone-grafts.—(*a*) *With Pedicle.*—Under this heading come for example thin bone flaps with the periosteum saved, and slid or twisted so as to fill a gap where there is lack of bony substance: non-union of a fractured tibia, as a most frequent instance, with necessarily shortened and freshened bone ends, leaving a gap.

Also under this heading, we may instance a very old method, namely, Gritti's operation; first done in Milan in 1857. This consists in amputating at the knee, sawing away the articular surface of the patella, and across the femur at as low a level above the condyles as about corresponds in circumference with the patella, and holding these two sawn surfaces firmly in apposition. In Gritti's time the mortality from bone infection caused it to be dropped; but in these aseptic times it has been brought forward again

with great success. It is the ideal method at the knee, for its stump best fits an artificial limb, and permits of comfortable end-bearing.

(*b*) *Without Pedicle.*—To discuss this method: We have to thank Macewen of Glasgow for first teaching us, many years ago, now, that bone will live when subdivided and devoid of its periosteum. He it was who first chiselled the discs of skull resulting from the activity of the trephine into a number of smaller bone-chips, and placing these side by side upon the dura found that vitalized plasma nourished them, at first by capillarity. Obviously, the denser the bone and the less possessed of a diploë, the greater its need to be minutely comminuted—for the capillarity will have the shorter distance to penetrate the bone and keep it vitalized.

Where the trephine is not used— and this is now most often the case—and it is contemplated to place side by side the bone pieces removed, perhaps the best of all tools for this purpose is De Vilbiss' rongeur, for its bites are at once quite small and always of exactly one and the same size and shape. They fit together smoothly like a mosaic—and being kept in warm saline solution until the end of the operation are apt to live.

A second example under this heading is the writer's method of operating upon old cases of Colles' fracture with deformity. We shall not go into the full details here. It will be found described in Binnie's Operative Surgery, and elsewhere. But after the radius has been chiselled across at the point of fracture and the articular surface and styloid process forced down a sufficient distance, the ulnar shaft is sawed across at about its middle, and enough of a piece of it removed to fill the gap in the radius—after chiselling this bit of ulna into lesser fragments. The gap in the ulna is not wide, and is needed in order to allow the ulnar head to cease its subluxation.

To discuss bone-grafting in mass, one point worth remembering is that the bone-graft seems more apt to live if deprived of its periosteum. That is, that periosteum against periosteum does not do so well as periosteum in contact with bare bone. But where a long bone is to be grafted into place, for example, as E. Lexer[1] does, using most of a fibula to replace all but the upper end of the humerus, he preserves the periosteum of the fibula, clears out by curette its marrow, replacing it by an iodoform plug, like Mosetig-Moorhof's, and grafts it in place still warm from the amputated leg from which he has taken it.

Rovsing[2] in using the fibula in this way not only preserves its periosteum but also leaves surrounding it a kind of sheath of muscular tissue, about one centimeter in thickness.

Perhaps as striking and successful an instance under the present heading as can be named is the brilliantly successful operation of Albee of New York, who saws vertically through half a dozen or so spinous processes over the kyphos in a case of Pott's disease that is quiescent, and breaks these spines apart, leaving thus a series of V-shaped bony troughs. Into this long gap he fits a strip of tibia of similar length, obtained from the patient at the same operation. In consequence of the solid bony union between the rigid splint of tibia and the vertebral spines, a further extension of the deformity becomes an impossibility.

III. Heterogenous Bone-grafts.—In this class are grafts from living lower animals, such as from the radius or the femur of the rabbit—to replace slender bones such as our metacarpal or metatarsal, or phalanges—or using similar bones obtained from the dog, the sheep, or the calf, usually when the need is for much larger and longer grafts. In every respect such work is performed as if the grafts had been obtained from human subjects. Some of our most successful work is of this nature. Many authorities consider them somewhat less apt to live and to become permanently useful, however, than equally fresh grafts from healthy human sources (amputated limbs). One great point in favor of the former source of supply is that it is ever at hand; whereas seldom indeed is this true of the living human donor. Doubtless, in the future, cold storage methods of preserving human limbs, for grafting alike of bone and of soft tissues as needed, will come into general usage; the temperature being held for months if need be at a point just above freezing—and the graft well warmed-up in normal saline or other watery solution just before its employment.

The use of Senn's bone-chips comes under this heading, so far as having its source of supply in the lower animals is concerned; but the chips are no longer vitalized. Senn thus describes his method of preparation: "Select a compact layer of the fresh tibia or femur of the ox, remove all periosteum and medullary tissue, divide into longitudinal strips about one-eighth of an inch wide and immerse in a relatively large quantity of ten to fifteen per cent. watery solution of hydrochloric acid, which must be renewed daily, for from one to two weeks; then wash thoroughly in water or a weak solution of caustic potash, cut into small chips, soak for forty-eight hours in 1–1,000 watery mercuric bichloride solution. Remove and store in saturated solution of iodoform in ether. When about to be used, wrap in aseptic gauze, dissolve out the excess of ether and iodoform with alcohol—and put in 1–2,000 mercuric bichloride watery solution till required, when careful drying with iodoform gauze should precede their implantation."

Fill the sterilized bone-cavity entirely full of these chips. Treat exactly as in Schede's blood-clot filling method (see below). This blood flowing in beneath the dressings which are first put in place, solidifies the whole mass. The bone-chips act as a sort of support or trellis for the spread of the granulation tissue. The iodoform acts as a safeguard. There is always a risk that not every last one of the untold myriads of microbes active during the osteitis has been removed or destroyed; and the iodoform, while it is no direct poison at all to microbes—which multiply as readily in gelatin saturated with it as without it—yet neutralizes the poisons produced by their life activities and death decompositions. Hence the patient's leucocytic armies, no longer having to fight enemies using poisoned weapons, can readily overcome and devour them by phagocytic activity.

Under this same head, should probably be mentioned grafts carved from ivory. These have been used of all sizes—from a small ivory plug fitting closely into a corresponding bone-cavity, the skin being dissected loose and brought together, with every aseptic precaution, to a great piece carved to resemble the upper end of the femur, and playing in the well-oiled acetabulum. Its lower end, in this case, was fastened securely to the upper part of the femoral shaft. Similarly, an entire knee-joint has been carved from two pieces of ivory, and made secure to the sawn ends of the femur and the tibia. A fair degree of success has sometimes been obtained. The ivory never grows—never shows signs of living activity. But on the contrary in time the alkaline vital fluid may perhaps erode it to some slight degree; or possibly, since it is finally a little attacked, this may be by the nascent carbonic acid gas continually being formed in the blood, and which is probably the source whereby a sequestrum finally is dissolved enough to become loosened from the living bone. It is conceivable that in like manner the nascent CO_2 may attack the ivory.

IV. Plastic Bone-fillings.—(*a*) Under the heading of plastic bone-filling from live sources come the following two methods. *First:* Neuber's deep canalization. In this we first operate to remove the sequestrum, chisel away sharp edges of bone—but leave all perios-

teum possible—and sterilize most carefully the living bone-surface, deprived of its covering of granulations; then, applying Neuber's method, we dissect up the skin and subjacent tissues from the muscle upon both sides of the wound, until, as nearly as possible without undue tension upon the skin, its edge is made to meet the opposing skin-edge at the bottom of the cavity in the bone. It is held thus in place, on both sides, by stout retention-sutures, *plus* a gauze packing lightly placed, or else the flaps are actually nailed down to the bare bone.

By this plan the patient is often enabled in a fortnight or so to leave the hospital, with only a deep sulcus, skin-lined, to indicate the site of his necrosis. And because of the striking tendency on the part of nature toward bringing up the skin to the surrounding level, little by little connective tissue and finally bone forms at the bottom of the depression; until after a year or longer, depending upon the degree of deformity, little indeed will remain to indicate where this device was used.

Second: Schede's filling by live blood-clot. The most frequent instance where this is employed is following excision of the head of the first metatarsal bone for radical cure of bunion. The steps are as follows:

1. Absolute surgical cleanliness. No operation is more certain to be a lamentable failure than Schede's blood-clot filling whenever used, where there is the least break in the "chain of asepsis."

2. Cording the thigh, for bloodless work.

3. The writer's choice of incison here is U-shaped, wide at the top to allow plenty of circulation in this skin-flap; and this incision allows room for work.

4. With a Gigli wire saw remove the entire head of the first metatarsal bone. The sesamoid bones are not to be touched; neither is any other structure within the wound save as stated.

5. Closure by a few interrupted catgut stitches: interrupted, to allow escape into the gauze dressings of any blood which may flow in excess.

6. Dressing, a principal feature of which should be a narrow, gauze-padded, thin wooden splint, along the sole and protruding a centimeter or two beyond the great toe end. Also, a gauze sponge is placed between the first and second toe, to overcorrect the deformity somewhat.

7. Sterile oil-silk or other impervious covering—and then plaster of Paris, covering all and extending nearly to the knee.

8. Let up on the rubber tubing and elevate the limb.

Blood will take the place of the excised bony head, and will proceed to become organized into new bone with a speed surprising to one not familiar with what can be done in this way. Only in two ways can failure result—through infection, or in consequence of insufficient bleeding, whereby the bone is but partly replaced.

In this particular instance the blood-supply is always enough for the purpose, so far as we are aware.

For three weeks, upon the average, the patient should remain in bed, or at least with his foot always elevated as high as the level of the hip. During a second period of three weeks he can walk about in his plaster cast. When six weeks have thus elapsed, the dressings can be removed. During this latter half of the time *post operationem* it will be well to prescribe lactate of calcium in as full doses as the stomach will tolerate. (This is not mentioned by Schede.)

Under (*b*)—from other than living sources and plastic—we may name the following:

1. Mosetig-Moorhof's iodoform wax plug. This has the following composition: Iodoform, 60 parts; spermaceti, 40 parts; oil of sesame, 40 parts. Heat slowly to 100° C. It is a soft solid at bodily temperature. When about to be used heat it to 60° C. to render it fluid. Fill the sterilized and *dry* bone-cavity completely with it. Two chief ways are our choice, to stop oozing of blood. We may try boiling water, avoiding its touching the skin, and leaving the bone-cavity thus filled but ten to twenty seconds. A temperature of 100° C. (212° F.) is far safer than a lower one, for it coagulates any blood in quicker time. Or else we may pump in hot air.

2. Neuber's iodoform starch. Mix ten grams of wheat starch with the smallest possible amount of water in an open vessel; pour into this, stirring constantly, two hundred grams of boiling 2 per cent. watery carbolic solution. After partial cooling stir in ten grams of powered iodoform. Pour into a sterile glass flask. This mixture may be kept for weeks in a dark room. Use as with Mosetig-Moorhof's method. (Note: iodoform as purchased in the market is by no means always sterile. The surgeon should purify it before use—otherwise he may perhaps convey microbic enemies and their antidote at the same time into the wound.)

3. Prepared beeswax. This, as a means of controlling bleeding from small vessels in bone, is old indeed. When solid it is thus rubbed into the oozing cancellous tissue—and the bony-cavity now quite dry is filled with the same agent melted. Ordinary beeswax, first sterilized by heat, has been used, but is more generally modified by one or another additional substance. The following is a favorite form of it: Take bleached beeswax to which Venice turpentine has been added to render it less crumbly to the touch. This comes in thin sheets, as used by makers of artificial flowers. A convenient way is to melt and sterilize this in large urinary test-tubes; keep well corked, with melted beeswax to seal the cork air-tight. Beeswax is absorbed and removed in a few weeks or months time. This also is true of the two methods described before this and the next two to follow.

4. Paraffin. This is commonly divided into two kinds, hard and soft—though all gradations are found between. The latter is absorbed in some months; the hardest paraffin, melted and hardening again in place, is either absorbed only after years or not at all.

5. Emil Beck's Paste. This very valuable mixture has been used the world over successfully to fill sinuses of all kinds, as well as cavities in bone. It is also often modified in composition. However, the following is the original formula, the one most used: Bismuth subnitrate, 30 parts; yellow vaseline, 60 parts; soft white paraffin, 5 parts; beeswax, 5 parts. This is heated to sterilize it, and resembles pea-soup in appearance. It quickly hardens in the wound, and at bodily temperature is solid. There is no danger, now-a-days, from arsenic poisoning, we learn; bismuth, as sold by any responsible dealer, is free from it. However, there have occurred a few cases of nitrite poisoning from the use of large amounts in this way of bismuth subnitrate. Hence, it has been advised to substitute the subcarbonate of bismuth for it.

6. Plaster of Paris, sterilized first by heat and stirred in water simply sterile or mildly antiseptic, to the consistency of thin cream—carefully avoiding air-bubbles. This quickly sets to stony hardness.

7. For very small bony cavities, after their due preparation as already repeatedly specified, either amalgam may be used, just as prepared by dentists, or else

8. Oxychloride of zinc, likewise employed by dentists mainly for temporary fillings in teeth, has been successfully used in instances under the present headings.

9. Dental guttapercha, being remarkably non-irritant, is worth a trial. ROBERT H. M. DAWBARN.

REFERENCES.

[1] Archiv f. klin. Chir., lxxxv., 939.
[2] Hospitalstidende, iii., No. 1. Ref. Journ. de Chir., March, 1910.

Bone-Setting.—In every country there is a class of irregular practitioners who make a living, and sometimes also quite an extensive reputation, by their success in restoring functional usefulness to crippled limbs. These individuals are, as a rule, most arrant quacks, knowing absolutely nothing of anatomy, or of the pathology of the conditions which they are called upon to treat, and yet they are often successful to a remarkable degree in curing certain joint affections which may have baffled the skill of the most experienced and able surgeons. These men are known as bone-setters, from their invariable assertion, made often through honest ignorance, that "the bone is out of joint, and only needs to be set." It is true that they frequently inflict most serious injury, which may lead to loss of limb or life itself, yet it is also undeniable that they sometimes restore a limb which might otherwise remain permanently crippled, or even be sacrificed as a useless incumbrance.

Dr. Wharton P. Hood[1] was the first to study intelligently the methods employed by bone-setters, and it is to him that most of our knowledge of this art, for art it is, though no science, is due. He defines bone-setting as "the art of overcoming, by sudden flexion or extension, any impediments to the free motion of joints that may be left behind after the subsidence of the early symptoms of disease or injury; perhaps, indeed, more frequently of the latter than of the former." The cases that most frequently fall into the hands of bone-setters, and are cured, to the joy of the patient, but to the discredit and loss of reputation of the regular practitioner, are those of slight fibrous ankylosis, of a degree sufficient to limit motion and impair the functional utility of the limb, yet not such as apparently to demand forcible rupture, an operation so unreasonably dreaded by many surgeons. In such a case, perhaps, some feeble attempts at passive motion are made. The joint is flexed cautiously and slowly, until the patient complains bitterly of pain; then the operator desists, orders the limb to be kept at rest, and bathed with lotions to subdue the inflammation excited by the strain put upon the adventitious bands. A few days later, when the heat and swelling have disappeared, the same manipulations are repeated, and followed again by inflammation and its treatment. After a number of repetitions of this sort the patient sees that he is no better than before, and refuses to submit his joint to any further manipulations. Then he becomes discouraged, limps around with the aid of a cane or crutches, and tries to bear philosophically the thought that he is a cripple for life. But at last some friend tells him of a wonderful cure performed by a bone-setter in a case apparently similar to his own, and in desperation he sends for the quack. The latter assures him that the bone is out and only needs to be replaced. He orders the joint to be enveloped for a time in flaxseed poultices, probably a procedure that contributes in no way to the success of the operation, and then on the appointed day meets his patient, seizes the limb, and with a quick motion flexes and extends the joint to its full extent, breaking up all the adhesions, and the patient finds that he is cured. The pain of the operation is but little greater than that inflicted by the regular practitioner in his feeble and ineffectual attempts to restore motility, and the resulting inflammation is usually slight or nil. The quack says that the bone is restored to its place, pockets his fee, and retires with glory.

This is no exaggerated picture, but is a true tale of what actually occurs in not a few instances, as many practitioners will sorrowfully admit. The good that bone-setters do is in these cases of partial ankylosis, and it is because they are unable to discriminate between the different conditions in which joint motion is impeded that they so often inflict irreparable injury. No surgeon would attempt forcibly to move an articulation which is the seat of strumous or tuberculous inflammation, yet this is what the bone-setter does with dire result. In most of the joints which can be benefited by forcible movements there is a tender spot, usually about the inner side, for which the bone-setter always feels, and the discovery of which is to him a sign of ultimate success. The motion of the joint is not absolutely abolished, but is limited in certain directions, and any attempt to pass this limit causes pain. The skin over the articulation is not hot, and all the other signs of inflammation, except perhaps a slight serous effusion, are absent. The following is an enumeration of the location of these painful spots, together with Mr. Fox's explanations of their occurrence, as given by Mr. Edward Cotterell in a very practical little work treating of the minor injuries of the limbs.[2] 1. "Over the head of the femur, in the center of the groin, corresponding to the iliofemoral band of the capsular ligament (which is most severely stretched when the thigh is over-extended, as when the trunk is flung violently backward, the commonest cause of a sprained hip). 2. For the knee-joint, at the back of the lower edge of the internal condyle; in other words, at the posterior border of the internal lateral ligament, where it blends with Winslow's ligament, and where the semimembranous tendon is in intimate relation with it. These parts suffer most because, as Mr. Morris says, 'during extension they resist rotation outward of the tibia upon a vertical axis, and a sprained knee is almost always caused by a twist outward of the foot.' 3. For the ankle, on the front of the external malleolus, the apex of the plantar arch, and the tip of the fifth metatarsal bone. 4. For the shoulder, at the point corresponding to the bicipital groove, because in nine cases out of ten a man sprains his shoulder to prevent himself from falling; his hand grasps the nearest support, the body is violently abducted from the arm, the long head of the biceps is called upon to exert its utmost restraining power, the bicipital fascia is overstretched, and the tendon very often misplaced. 5. For the elbow, in front of the tip of the internal condyle; the fan-shaped internal ligament has its apex at that point, and it is most stretched in oversupination with extreme extension of the forearm. 6. For the wrist, the styloid process of the ulna, and the annular ligament in front of the wrist."

The bone-setter's manipulations consist in first locating the painful point, upon which the thumb is firmly pressed during the remainder of the operation; and then, while the operator steadies the proximal segment of the limb, the distal segment is grasped and rotated as much as possible on its axis in order to overcome, as far as may be, muscular resistance; this being accomplished, the joint is sharply flexed or extended in the direction of greatest resistance, and then the reverse movement is made until all the adventitious bands are broken, or until the "bone is put back," in the bone-setter's own phraseology. The rupture of these bands of adhesion is often accompanied by a loud report. For a description of the special manipulations required for each joint, the reader may consult the work of Wharton Hood, above referred to. T. L. S.

References.

1. On Bone-Setting (so-called), and Its Relation to the Treatment of Joints Crippled by Injury, Rheumatism, Inflammation, etc. By Wharton P. Hood, M.D., M.R.C.S., London and New York, 1871.

2. On Some Common Injuries to Limbs: Their Treatment and After-treatment, Including Bone-setting (so-called). By Edward Cotterell, M.R.C.S., Eng., L.R.C.P., Lond., London, 1885.

Bonet, Théophile.—(The latinized form, Bonetus, is also frequently employed by writers.) Born at

Geneva, Switzerland, on March 5, 1620. Both his father and his grandfather were skilful physicians, the latter having been the medical adviser of Charles Emmanuel, Duke of Savoy. On his mother's side he was descended from the illustrious Genoese family of Pinelli Borzoni, who had been driven out of his native city on account of his religious opinions, and had taken refuge in Geneva about the year 1612. Théophile Bonet pursued his medical studies with enthusiasm, visited all the celebrated universities of Europe, and took his doctor's degree in 1643. He settled in his native city, and in a very short time acquired an extensive practice. Henry of Orleans, Duke of Longueville and Prince of Neuchâtel, made him his medical adviser. About the year 1670, Bonet, who had been gradually losing his hearing, retired from practice and devoted himself during the remainder of his life to medico-literary work. He died on March 29, 1689.

According to Dezeimeris ("Dict. Hist. de la Méd.") the published writings of Bonet are quite remarkable in at least one respect; they contain, in a well-digested form, all the more important facts, ascertained before his time, in the domain of practical medicine. In the collection of these facts Bonet made it a rule to place on record only those cases in which a postmortem examination formed an integral part of the history of the malady. Of all the collections of a similar character made before the end of the seventeenth century, this one is by far the best; it bears the title: "Sepulchretum, sive anatomia practica, ex cadaveribus morbo denatis, proponens historias et observationes omnium pene humani corporis affectuum, ipsorumque causas reconditas revelans. Quo nomine, tam pathologiæ genuinæ quam nosocomiæ orthodoxæ fundatrix, imo medicinæ veteris ac novæ promptuarium dici meretur, cum indicibus necessariis," Geneva, 1679, 2 vols., in-folio (also an edition published at Lyons in 1700). The famous Haller speaks of Bonet's *Sepulchretum* as a work of imperishable value.

A. H. B.

Boophilus.—*Rhipicephalus.* A genus of ticks, family *Ixodidæ*. *B. bovis* is an intermediate host for the pathoganic microorganism of Texas cattle-fever. In this species the mother tick sucks blood from a cow and the eggs are each enclosed in a shell with some of this blood; hence the young may be already infected with the fever parasite when hatched. See *Arachnida*.

A. S. P.

Borage.—The leaves and flowering tops of *Borago officinalis* L. (fam. *Boraginaceæ*). An European or Oriental plant, occasionally cultivated in flower gardens in the United States. It has a succulent, branched, hairy stem, half a meter or so high (twenty inches), with rough, coarse-looking, entire leaves, and terminal one-sided cymes of pretty blue flowers. Borage has been a domestic medicine in Europe for years. Its odor is slight, at least when dry; taste, bland and mucilaginous. It contains no more active principles than mucilage and nitrate of potassium, and its medical qualities are only those of a mild demulcent.

H. H. Rusby.

Boraginaceæ.—A family of some eighty-five genera and nearly fifteen hundred species, very widely dispersed, but mostly in warm temperate climes. Except for ornamental purposes, especially the heliotropes and forget-me-nots, the family is but little utilized. Its chief use at present is to yield the coloring matter alkanna red. Historically, it is of considerable interest in medicine, the borage, comfrey, lungwort, eritrichium, viper's bugloss, and other drugs having formerly enjoyed a high, though ignorant repute. Although some of their alkaloids are quite active, they occur in inconsiderable proportions.

H. H. Rusby.

Borax.—This salt, $Na_2B_4O_7,10H_2O$, is official in the U. S. Pharmacopœia (8th Revision) as *Sodii Boras*, Sodium Borate. This name is not well chosen, for borax is not a salt of boric acid, but of pyroboric or tetraboric acid. The British Pharmacopœia gives as a synonym biborate of sodium, which is also confusing. The proper chemical designation for borax is evidently disodic tetraborate. It occurs in "colorless, transparent, monoclinic prisms, or a white powder, inodorous, and having a sweetish, alkaline taste. Slightly efflorescent in warm, dry air. Soluble in 20.4 parts of water at 25° C. (77° F.), and in 0.5 part of boiling water; insoluble in alcohol; it is soluble in one part of glycerin at 80° C. (176° F.). When heated, the salt at first loses part of its water of crystallization, then melts, and, when further heated, swells up and forms a white, porous mass. At a red heat it loses all of its water of crystallization (forty-seven per cent.), and fuses to a colorless glass. To a non-luminous flame it imparts an intense yellow color" (U. S. P.). Borax occurs native on the shores of certain lakes, and as a crystalline deposit at the bottom of the Borax lake in California. It is also made from boric acid and sodium carbonate: $4H_3BO_3 + Na_2CO_3 = Na_2B_4O_7 + CO_2 + 6H_2O$.

Borax is locally bland and constitutionally innocent, and its medicinal virtues seem to reside in the combination of feeble alkalinity with a slight degree of antiseptic power derived from its acid radical. Borax acts well as a mild detergent alkali in skin diseases or catarrhs and ulcerations of mucous membranes, particularly of the mouth. A lump held in the mouth and slowly sucked seems to excite the secretions of pharynx and larynx, and in case of huskiness from dry catarrh of these parts temporarily restores something of the natural quality to the voice—an important matter to a singer or speaker affected with a cold. Internally, borax may be used as a feeble alkali, and may be given in doses of gr. v.–xv. (0.30 to 1.00); externally, it may be applied in lotions ranging from one to five per cent. in strength (limit of solubility in water), or in ointment of thirty-per-cent. strength. Although slightly antiseptic, borax has practically no germicidal powers. Its chief use is as gargle or mouth wash in stomatitis or aphthæ; and also as a lotion in conjunctivitis.

R. J. E. Scott.

Bordighera.—A marine health resort on the Mediterranean coast of France, ten miles east of Mentone and three miles west of the Italian boundary.

"Bordighera is a conspicuous object nearly all along the western Riviera, as it is seen glittering in the sunshine, its houses clustered together on a promontory that projects far out into the sea. It is the only health resort on this coast that occupies a position on a promontory; all the others being built round bays or depressions in the coast. It is naturally, therefore, much exposed to winds, that is to say, to all those winds that can reach it in blowing across the sea; the east, the southeast, the southwest, and the west winds can all blow freely upon this promontory. But it is well protected by mountains to the north, northeast, and northwest, whence the coldest winds come. Moreover, it must be remembered that all the winds that reach it must, on account of its position, come to it from the sea, and impregnated with saline emanations. And this is the sole distinguishing characteristic of the climate of Bordighera as compared with that of neighboring stations; the predominating influence of sea air rendering it essentially bracing and tonic" (Burney Yeo).

Bordighera is a small town of 2,500 inhabitants, and the portion devoted to invalids is called the "new town," or English quarter, and is on level ground to the west of the promontory. The hotels and villas

are surrounded by groves of olive, lemon, and palm trees. The latter grow to a great height and are said to be more plentiful than in any other part of the Italian Riviera. "It is said that there are more palms in the neighborhood of Bordighera than in the whole of Palestine" (Dean Alford). The natives have a monopoly of supplying the Vatican with palm leaves for Palm Sunday. Dense olive groves also cover the plain upon which the new town is situated. The drainage of the town is primitive, but the place is said to be healthy, and the hygienic conditions are considered good. The water supply is obtained from wells, and from a spring in the flank of Monte Nero (Goodchild). During a residence of fifteen years Dr. Goodchild has seen no case of typhoid fever or diphtheria among the members of the English colony.

The average monthly temperature for the months from October to May inclusive is as follows:

Mean Temperatures, 1876–79.

October	63.5° F.	February	49.1° F.
November	55.0° F.	March	50.5 F.
December	49.0° F.	April	55.1° F.
January	49.6° F.	May	61.0° F.

The temperature averages about three degrees lower than that of Mentone, according to Dr. Goodchild, and the range is smaller. The relative humidity approximates to that at San Remo, which has a yearly average of 66.7 per cent. The rainfall also is about the same as at San Remo, at which place the number of days on which rain falls during the season is thirty. "At Bordighera the mistral is the west wind, being turned completely in that direction by the mass of mountains behind Monaco, and from being forced to blow over the sea it loses somewhat of its dry and cold character" (Burney Yeo). "The soil upon the hillsides is limestone and conglomerate, but upon the flat it is composed of old sandy sea beaches, in which the water rapidly finds the sea level. About a couple of acres near the English church possesses a soil, however, in which there is a small admixture of clay and which is somewhat damp in consequence" (J. A. Goodchild, M. D.).

The climatic characteristics of Bordighera can be summarized as those of a Mediterranean health resort, affording pure sea air, a mild equable winter temperature, a comparatively low relative humidity, and, in common with the other resorts of the Riviera, a large amount of sunshine. Thus, an outdoor life in a mild bracing sea air is afforded. The variety of level shady walks among the palms and olive trees, and the attractive excursions in the neighborhood add a charm and interest to the invalid's life there.

The class of diseases which are likely to be benefited by this climate are those requiring a warm, moderately moist sea climate. As has been said before (*vide* note upon *Algiers*), a climate of this character is not an especially curative one for phthisis, and all that can generally be expected of it in this disease is to ameliorate symptoms and prolong life. Strumous cases, especially in children; patients with anemia, diabetes, or albuminuria; convalescents from acute diseases; the weak and debilitated; sufferers from chronic bronchial catarrh, from catarrh of the stomach and intestines, and from various other conditions of constitutional feebleness, find here a suitable climate—"cheering to the mind and invigorating to the body."

Bordighera is not suitable for the febrile and for those who are very nervous and sensitive. The accommodations are said to be very comfortable, although somewhat limited. "English tastes are consulted, as nearly all the visitors are English or Americans" (Ball). There are English physicians, a reading room and free library.

Bordighera may be reached viâ Marseilles, or by way of Turin and Savona. By the former route it is thirty-three and a quarter hours distant from London. Steamers also sail direct from New York to the Riviera during the Season.

Edward O. Otis.

Boric Acid.—This substance (H_3BO_3), often called by the older but less correct name of *boracic acid*, is official in the United States Pharmacopœia under the title *Acidum Boricum*, Boric Acid. It is described as "transparent, colorless scales, of a somewhat pearly luster, or six-sided, triclinic crystals, or a light, white, very fine powder, slightly unctuous to the touch; odorless, having a faintly bitter taste, and permanent in the air. Soluble in 18 parts of water, in 15.3 parts of alcohol, and 4.6 parts of glycerin at 25° C. (77° F.); in 3 parts of boiling water and 4.3 parts of boiling alcohol. The addition of hydrochloric acid increases its solubility in water. An aqueous solution of boric acid (one in fifty) colors blue litmus paper red." (U. S. P.) It is usually prepared by the action of hydrochloric acid on an aqueous solution of borax. It should contain not less than 99.8 per cent. of pure boric acid.

Boric acid is a very feeble acid chemically, and physiologically lacks the ordinary acid qualities of sour taste and tendency to irritate. Even a saturated aqueous solution is tasteless, and without irritant action on so sensitive a part as the conjunctiva. Constitutionally, also, in all ordinary applications, the drug is harmless; but yet poisoning and even death have followed, in a few cases, a very extensive use of the acid. The essential symptoms in such cases were nausea, vomiting, hiccough, feeble heart action, and fall of temperature, with the development of an erythematous rash, affecting particularly the legs.

Boric acid is a mild antiseptic—convenient withal, because odorless, tasteless, unirritating, and non-poisonous in ordinary application—but must not be relied upon as a germicide in the proper understanding of the term. Probably because of its antiseptic action, boric acid, locally applied, tends to abate the catarrhal process, and is, for such application, peculiarly agreeable because non-irritating. As a collyrium in conjunctivitis, a gargle in pharyngitis, or an injection in cystitis, a solution of boric acid is, therefore, often efficacious, and at least innocent of harm. For an application to catarrhal surfaces, or for antiseptic purposes to wound surfaces, boric acid may be used in aqueous solution ranging from one to four per cent. in strength—the latter being, indeed, at ordinary temperatures, a saturated solution.

A stronger solution, if wanted, is obtainable by using a mixture of equal parts of boric acid and borax, which dissolves to the extent of sixteen per cent. in water at ordinary temperatures. A convenient and efficient wound dressing may be made by soaking lint in a hot saturated aqueous solution of boric acid, and then allowing it to dry. A boric-acid ointment also has been recommended, where, to a melted mixture of one part each of white wax and spermaceti and six parts of vaseline, is added a proportion of from two to four parts of a saturated solution of boric acid in glycerin. Also the substance *boroglycerin* (*q.v.*) affords a means of applying boric acid in strong solution. The pharmacopœial dose is gr. viiss. (0.50); but boric acid has also been given internally in doses of gr. xxx. (2.0) frequently repeated, with no poisonous effect, and with asserted benefit in fermentative dyspepsia, in chronic cystitis, in diphtheria, and in other diseases probably due to microorganisms. It is also used as a food-preservative.

Edward Curtis.
R. J. E. Scott.

Borland Mineral Well.—Pleasants County, West Virginia. The well from which the Borland Mineral water flows is situated on the bank of Blue Creek, six miles from Willow Island, West Virginia, on the Ohio River Railroad, and twenty-two miles northeast of Parkersburg. There are good hotel accommodations and nearby farmhouses accommodate a limited number of guests who wish to use the water from the well. Persons desiring to come to the springs will be met by a conveyance at Willow Island if word is sent in advance. The surrounding hills and valleys present some very pleasing landscapes. The water rises from a flowing well, being forced upward by the natural-gas pressure from a depth of three hundred feet. An analysis by Prof. T. G. Wormley of Philadelphia showed the following mineral ingredients:

One United States Gallon Contains:

Solids.	Grains.
Sodium chloride	240.07
Sodium bicarbonate	112.19
Sodium sulphate	37.87
Magnesium bromide	0.28
Potassium sulphate	22.62
Magnesium iodide	0.28
Magnesium chloride	2.14
Calcium bicarbonate	12.39
Magnesium bicarbonate	3.13
Aluminum phosphate	0.23
Aluminum and iron carbonate	0.64
Manganese	Trace.
Silica	0.58
Organic matter	Trace.
Total	432.42

Sulphureted hydrogen.....A perceptible quantity.

The following estimations supplementary to the Wormley analysis have been made on the Borland mineral water at the West Virginia experiment station:

One United States Gallon Contains:

Solids.	Grains.
Sodium sulphide	0.39
Manganese carbonate	0.01
Lithium chloride	Trace.
Ammonium chloride	0.98
Albuminoid nitrogen	Trace.
Gases, cubic inches per gallon:	
Free carbonic acid	9.93
Carbonic acid in bicarbonates	99.28
Sulphureted hydrogen	0.41
Carbureted hydrogen	present.
Dissolved oxygen	0.66
Temperature	55° Fahrenheit.

This water is quite a strong muriated, alkaline saline. It is a very efficient antacid laxative, with diuretic and diaphoretic properties. It also derives a certain tonic and restorative influence from the presence of iron, phosphorus, and manganese. In addition to its table value it has been found to possess excellent therapeutic properties in chronic affections of the stomach, bowels, liver, and kidneys. It acts with great efficacy in renal dropsy; also in asthma and rheumatism. Emma E. Walker.

Borneol.—*Borneo Camphor; Dryobalanops Camphor* ($C_{10}H_{17}-OH$). A camphor-like body occurring in the wood, and in lumps in the cavities thereof, of *Dryobalanops aromatica* Gaertn. (fam. *Dipterocarpaceæ*), in a number of *Coniferæ*, in valerian, rosemary, and several other aromatic plants. The article is not exactly the same, differing especially in its optical properties, from these different sources. That commonly sold is artificially made from ordinary camphor by the action of sodium. This differs from ordinary camphor in its much higher melting- and boiling-points, and in not crystallizing upon the sides of the glass containers. It is crystalline and soluble in alcohol. It is used externally as a disinfectant to sores. H. H. Rusby.

Boroglycerin.—Under this title there has been introduced into medicine a compound formed by direct reaction of boric acid upon hot glycerin. In this reaction the BO_3 of boric acid replaces the three hydroxyl equivalents of the molecule of glycerin, forming *glyceryl borate*, $C_3H_5BO_3$, with evolution of water, as per the following equation: $C_3H_5(OH)_3 + H_3BO_3 = C_3H_5BO_3 + 3H_2O$. Boroglycerin is a solid, vitreous body, transparent, and of a light amber color. It has little odor, and a slightly sweetish taste, with a faint astringent twang. It is hygroscopic, rapidly becoming sticky on exposure to the atmosphere. It dissolves freely in glycerin, and, melted into an equal weight of that fluid, forms a permanent, viscid, clear solution. The solubilities in water and alcohol have been stated very variously. A sample tested by Edward Curtis broke up into opaque, granular flakes by treatment with cold water, but finally dissolved in ten times its weight of that fluid; and in cold absolute alcohol it dissolved slowly but completely, in even less than its own weight, forming a clear, syrupy solution.

Boroglycerin is reported to be antiseptic, and was originally proposed as an agent for the preservation of food-stuffs. Taken internally it has seemed to be as innocent as the two substances of which it is compounded. It has so far been used in medicine locally only, being applied—generally in glycerin solution—as a dressing to wounds, ulcers, catarrhal mucous membranes, etc. It is claimed to be at once antiseptic, astringent, and healing, while inodorous and practically unirritating. It is most commonly employed in fifty-per-cent. glycerin solution, or in ointment made by mixing one part of such glycerin solution, while hot, with three parts of vaseline. A glycerin solution of boroglycerin is official in the United States Pharmacopœia, under the title *Glyceritum Boroglycerini*, Glycerite of Boroglycerin. In this case the solution is made directly by treating 310 grams of finely powdered boric acid with enough hot glycerin to make 1000 grams. The directions given in the U. S. P. are: "Heat 460 grams of glycerin, in a tarred porcelain dish, to a temperature not exceeding 150° C. (302° F.), and add the boric acid in portions, constantly stirring. When all is added and dissolved, continue the heat at the same temperature, frequently stirring, and breaking up the film which forms on the surface. When the mixture has been reduced to the weight of 500 grams, add to it 500 grams of glycerin, mix thoroughly, and transfer it to suitable vessels." The preparation is a colorless, glycerin-like fluid.

As a preservative, boroglycerin has been recommended in solutions ranging from two per cent. to five per cent. in strength. R. J. E. Scott.

Borthwick Mineral Springs.—Also known as the Ottawa Mineral Springs.

Post-office.—Ottawa, Canada.

Access.—By carriage drive from Ottawa.

Analysis.—By I. Baker Edwards.

One Pint Contains:

Solids.	Grains.
Chloride of sodium	98.081
Chloride of potassium	1.310
Chloride of calcium	1.832
Chloride of magnesium	2.713
Bromide and iodide of magnesium	0.351
Sulphate of calcium	2.019
Sulphate of magnesium	2.450
Sodium, bromine	Traces.
Total	108.756

This is an unusually pure saline water, containing a large percentage of iodine and bromine. A small amount of purgative salts is also present, forming an excellent combination. There is no aëration with carbonic acid. These waters are extensively used by the residents of Ottawa and vicinity.

BEAUMONT SMALL.

Boston.—Massachusetts. Although this and various other cities which will be mentioned in the HANDBOOK are not health resorts, yet it frequently happens that an invalid is obliged, from reasons of necessity, to spend more or less time in them, and it is a satisfaction to know something of the climate and weather which may be expected. Further, as Dr. Huntington Richards, the previous editor of this department, says: "One can better form an opinion of the climate of any health resort he may have under consideration, if he compares it with that of the place in which he resides or with that of some place with which he is familiar." For these reasons, then, the climatic tables and general weather conditions of the principal cities of the United States will be given.

The climate of Boston is characterized by great variability and range, from a possible maximum of 101° F. in July to −13° F. in January. The east winds, although not the prevailing ones, as the climatic table indicates, are still frequent enough to form one of the peculiar characteristics of this climate. They are damp and chilly in winter and early spring, and render outdoor existence exceedingly uncomfortable.

> "A chill no coat, however stout,
> Of homespun stuff *can* quite shut out—
> A hard, dull bitterness of cold."

In the summer, on the contrary, they modify the heat and are very refreshing. Ask any inhabitant what is the one striking climatic peculiarity of Boston, and he will immediately reply, "The east wind."

CLIMATE OF BOSTON, MASS. LATITUDE, 42° 21′; LONGITUDE, 71° 4′. PERIOD OF OBSERVATION, FROM 13 TO 25 YEARS. ELEVATION OF PLACE OF OBSERVATION ABOVE SEA LEVEL, EIGHTEEN FEET.

Data.	Jan.	Mar.	July.	Year.
Temperature (Fahrenheit Scale)				
Average or normal.....	27.0°	34.2°	71.3°	48.2°
Average daily range.....	17.2	16.5	17.9	
Mean of warmest (average maximum).	35.3	42.2	80.8	
Mean of coldest (average minimum).	18.1	26.7	62.9	
Highest or maximum .	70.0	72.0	101.0	
Lowest or minimum	−13.0	−7.5	46.0	
Humidity				
Mean relative (average).....	71.8%	69.4%	70.8%	69.6%
Wind				
Prevailing direction. . . .	N. W.	N. W.	W.	W.
Average hourly velocity in miles.	12.2	11.3	8.5	
Weather				
Average number of clear days.	8	8.7	8	103
Largest number of clear days.	13	..	15	
Smallest number of clear days.	4	.	3	
Average number of fair days..	10.6	9.5	13.7	134.6
Largest number of fair days..	15	.	20	
Smallest number of fair days.	7	.	3	
Average number of cloudy days.	12.4	12.5	9.4	135
Largest number of cloudy days.	19	.	23	
Smallest number of cloudy days.	7	.	3	
Average number of rainy days, .01 inch and over.	12.2	13.7	11	130
Smallest number of rainy days	4	.	6	
Largest number of rainy days	18	.	17	

The cold season begins in November, although it is occasionally mild even to Christmas, and continues until April; snow is for a great part of this time upon the ground, although not always continuously. March, on account of the high cold winds, is one of the most disagreeable months of the year, and June one of the most delightful, although the latter part of the month may be uncomfortably hot. In the summer, the heat, oppressive at times on account of the dampness, is not continuous, and in the writer's experience, from a climatic point of view, the spring and summer are the best seasons to spend in the city, and January, February and March, the months to be avoided by a change to a milder climate. Fashion, however, has it otherwise. The writer recalls the case of a family whose members had come on from St. Louis, in search of an Eastern seaside resort, but who, on arriving in Boston, had found the place so comfortable that they decided to remain there the whole summer.

The excursions by water are numerous and very delightful, and the country around is easily accessible and attractive. Boston is noted for its beautiful suburbs.

EDWARD O. OTIS.

Botalli, Leonardo.—Botalli, or Botallo, was born in Asti, Piedmont, in the early part of the sixteenth century; received the degree of Doctor of Medicine from the University of Pavia; visited Paris about the year 1564; and later served as physician to various royal personages—Charles IX, the Duke of Alençon (fourth son of Henry II), and Henry III. His name has been handed down to posterity chiefly because he is credited with the discovery of the opening of communication between the two auricles of the fetal heart (the ductus arteriosus) and also because he was the first to employ blood-letting with a degree of freedom previously unknown. As a matter of fact, however, the opening between the two auricles of the heart in the fetus had previously been seen and described by Galen, Vesalius and Aranzi (Dict. Hist. de Méd.). The book in which Botalli described the opening bears the title: "De via sanguinis a dextro in sinistrum cordis ventriculum," Venice, 1640.

A. H. B.

Bothriocephalidæ.—A family of tapeworms in which the bothria, or adhesive organs, are slit-like furrows; the proglottids are generally distinct and drop off in goups. The genus *Bothriocephalus* contains important parasites. See *Cestoda*. A. S. P.

Bothriocephalus.—A genus of tapeworms, family *Bothriocephalidæ*, which contains many parasites which occur as adults in man and other vertebrates. *B. latus*, in the intestine of man, may reach a length of twenty or thirty feet and have as many as 3,000 proglottids. The larvæ of this species swim in fresh water; pike and other fish are the intermediate hosts. See *Cestoda* A. S. P.

Bothrops.—*Lachesis*. A genus of very poisonous snakes which are without a rattle; it contains about forty species. The Fer-de-Lance, *L. lanceolatus*, is said to be more poisonous then any other snake; it is common in parts of Mexico and the Antilles.

A. S. P.

Botkin, Sergei Petrovich.—Born in Moscow, Russia, in 1832. His preliminary medical studies were carried on in his native city, but, after the fighting at Sevastopol came to an end (1856), he continued his medical studies in Paris (under Claude Bernard), and in Berlin (under Virchow, Traube, and Hoppe-Seyler). He received the degree of Doctor of Medicine

in 1860, and was almost immediately afterward made Professor of the Medical Clinic in the Medico-Military Academy of St. Petersburg. His death occurred on December 24, 1889, a short time after he had resigned his professorship. (Pagel.)

As a teacher Botkin was most stimulating, and his pupils held him in the highest esteem; as a diagnostician he was remarkably strong. His published writings will be found partly in Russian periodicals and partly in Virchow's *Archiv*. The titles of two of his German articles are as follows: "Ueber die Wirkung der Salze auf die cirkulierenden roten Blutkörperchen," Virchow's *Archiv*, xv., 1858; and "Zur Frage von dem Stoffwechsel der Fette im tierischen Organismus." A. H. B.

Botryomycosis.—At the present day the existence of a botryomycosis in mankind is denied on many sides and this scepticism extends to a certain extent to botryomycosis in general, as far as the term connotes a specific disease. Instead authors speak of pseudobotryomycosis or granuloma pyogenicum, which they assign to the same clinical family as "granuloma simplex" and "granuloma telangiectodes." These growths all agree among themselves in having the histological structure of ordinary granulomatous tissue, and while the bacterial causation is not absolutely known it is believed to be the ordinary *Staphylococcus pyogenes aureus*, perhaps acting with weakened virulence. Clinically, the cases originally described as botryomycosis humanus, granuloma telangiectodes, etc., present lesions on exposed localities—fingers, face—which almost invariably follow traumas. These lesions are rapidly growing, soft masses, sometimes very rich in blood-vessels and comparable with strawberries, and easily confused at times with malignant growths. They have been noted in vaccination wounds. Although they may recur after removal, they are not malignant. These formations were at first believed to result from inoculation with a fungus, partly because they resemble an affection in horses having that causation. It is now generally held that these lesions are true tumors—proliferating angiomata—which often originate in minute nævi. If this is true, then trauma, infection, etc., are simply activating agents. EDWARD PREBLE.

Botulism.—See *Food Poisons*.

Bouchardat, Apollinaire.—Born in Lisle-sur-le-Serein, France, in 1806. He received the degree of Doctor of Medicine in Paris, in 1832. His studies were directed chiefly to chemistry and pharmacy, and for a long time he held the office of Head Apothecary in Hôtel-Dieu, Paris. He died in April, 1886, at the advanced age of eighty, but he continued to work with apparently unabated vigor up to the very end.

FIG. 859.—Apollinaire Bouchardat.

Of Bouchardat's numerous contributions to chemical, pharmaceutical, medical, and hygienic literature, it will not be practicable to mention here more than the following: "Eléments de matière médicale et de pharmacie," Paris, 1839; "Manuel de matière médicale, de thérapeutique et de pharmacie," fifth edition, 1873; "Nouveau formulaire magistral, etc.," nineteenth edition, 1874; and "De la glycosurie ou diabète sucré, etc.," second edition, 1883. In addition, Bouchardat edited the following publications: "Annuaire de thérapeutique, de matière médicale, de pharmacie et de toxicologie" (since 1840), Archives de physiologie, de thérapeutique et d'hygiène," etc. During the last years of his life his energies were specially directed to the completion of the two treatises which he had most at heart—"Traité sur la glycosurie," and "Traité d'hygiène publique et privée basée sur l'étiologie," 1881. (Pagel.) A. H. B.

Bouchut, Eugène.—Born in Paris, France, May 18, 1818. In 1842 he received the degree of Doctor of Medicine, and in 1856 he was appointed an attending physician of the Hôpital Sainte Eugénie and the Hôpital des Enfants Malades. At this time he introduced a method of intubation of the larynx in diphtheria, but his instruments were crude and the practice was made the subject of so much ridicule by his colleagues that he was forced to abandon it. He died in November, 1891.

Bouchut was a prolific writer, chiefly on subjects belonging to the domain of pediatrics. His three larger works bear the following titles: "Traité des maladies des nouveau-nés, des enfants à la mamelle et de la seconde enfance," seventh edition, Paris, 1879; "Hygiène de la première enfance," seventh edition, 1879; and "Clinique de l'hôpital des enfants malades," Paris, 1883. (Pagel.) A. H. B.

Boulder.—A town in Colorado of 4,000 inhabitants, situated at an elevation of 5,300 feet above sea level, in the heart of the Rocky Mountains, thirty miles northwest from Denver. "The town is situated close to the foothills near the entrance to the Boulder Cañon" (Solly). The soil is dry and porous, except in areas of clayey soil. The water supply comes from a reservoir on Boulder Creek, five miles above the town, and also from wells, springs, and the creek itself. The hotels are said to be fair (Solly).

Although the meteorological data for Boulder itself are very incomplete, so far as the writer has been able to learn, they cannot be very different from those at Denver, thirty miles away (see article on *Denver*). Solly gives the mean monthly temperature for Boulder, from observations extending over a period of one year and a half, as follows: Winter, 30° F.; spring, 49° F.; summer, 65° F.; autumn is not obtainable. The average number of cloudy days during the winter is thirteen.

Boulder is one of the many representative places in the great high-altitude, health-resort belt of the Rocky Mountains, extending from Wyoming south along the eastern base of the Rocky Mountains, through Colorado into New Mexico, and then turning southwest into Arizona. "In this belt no particular spot is materially better than another, so far as climatic conditions are concerned" (Report of the Committee on Health Resorts. Transactions of the American Climatological Association, 1895).

Boulder, like many other localities in this belt, would seem to offer an almost ideal climate for the high-altitude treatment of phthisis: almost constant sunshine—but thirteen cloudy days on an average during the winter, clear bracing air, low relative humidity, nights that give invigorating sleep and rest, and grand mountain scenery. But it is well to repeat what has been before said, that climate is but one factor, although an exceedingly important one, in the treatment of phthisis, and in order to obtain the greatest advantage from any climate, however ideal, there must be at hand proper hygienic conditions and

wise medical supervision. Phthisical patients in health resorts require, as a rule, constant guidance and restraint; they must know when to practise the *rest cure*, and when it is safe to take exercise and how much, hence for many persons the well-conducted sanatorium is the only safe place.

EDWARD O. OTIS.

Boulder Hot Springs.—Jefferson County, Montana. POST-OFFICE.—Boulder. Hotel.

These springs are located within three miles of the town of Boulder, about midway between Butte and Helena. They are reached by the Great Northern Railroad. Automobiles meet all trains. The springs are numerous, and some of them have a large outflow of water. The surrounding country is of a rugged, mountainous character, the location of the springs being 4,975 feet above the sea level. The following analysis was made by Emil Starz, Ph. G.:

Solid matter.	Parts in 100,000.
Sodium sulphate	28.25
Sodium chloride	3.05
Potassium chloride	1.06
Calcium carbonate	1.56
Magnesium carbonate	0.19
Silica	8.35
Alumina	0.28
Iron	Traces
Total mineral solids	42.74

The temperature of the springs ranges from 125° to 187° F. The water is said to be very palatable as a beverage. The hotel is modern in all its appointments, and bathing facilities are abundant. The diseases especially benefited here are rheumatism, gout, indigestion, chronic constipation, renal, bladder, cutaneous, and hepatic diseases, and metallic poisoning.

EMMA E. WALKER.

Bourdet.—A surgeon-dentist who flourished in Paris, France, during the first half of the eighteenth century. In July, 1754, he published a letter in which he describes his method of treating cases of severe toothache. He first loosened or partially extracted the affected tooth, in order to rupture its nerve supply (the modern dentist accomplishes the same thing in a different and less painful way), and then, after pushing the tooth back into its alveolus, he proceeded to excavate the part that was decayed. In response to the hostile criticisms which soon reached him he published the following communication: "Eclaircissement de M. Bourdet, dentiste, du sujet de sa lettre adressée à M. D.," Paris, September, 1754. In addition to these two shorter communications Bourdet published three larger treatises—one on certain pathological conditions of Highmore's antrum ("Dissertation sur les dépôts du sinus maxillaire," Paris, 1754; 46 pp.), another on the pathology and treatment of dental affections ("Recherches et observations sur toutes les parties de l'art du dentiste," Paris, 1757; 2 vols.), and the third on the means by which one may readily keep the mouth clean and preserve the teeth from decay ("Soins faciles pour la propreté de la bouche et la conservation des dents," Paris, 1771; 248 pp.). Pierre Fauchard (*q. v.*), who is spoken of as the father of modern dentistry, published the first edition of his treatise in 1728.

A. H. B.

Bourgelat, Claude.—Born at Lyons, France, in 1712. He received his academic education from the Jesuit Fathers, and afterward studied law at the University of Toulouse. He commenced to practise his profession in Grenoble, and was soon successful in winning a case; but, knowing that his client was in the wrong, he felt only shame over his success, and as a result he immediately abandoned the profession of law, and became a member of the corps of musketeers. A great fondness for horses had been one of his marked characteristics since the time when he was a mere stripling, and, shortly after he had abandoned the law, he began taking lessons in horsemanship from the best teachers in Paris. The progress which he made caused general astonishment, and he, therefore, had no difficulty in securing an appointment as Chief of the Royal Academy of Equitation at Lyons. The school over which he presided soon became famous, and pupils flocked to it from every province in France, the great majority belonging to families of the nobility. Many also came from Denmark, Sweden, Prussia, Sardinia, and Switzerland. The welfare of the horse next occupied his attention; and, in order to obtain a thorough knowledge of the diseases to which this animal is liable, he carried on, for a number of years, the practice of making dissections at every possible opportunity. In addition, he studied human anatomy, pathology, and therapeutics, until he had achieved the reputation of being a most skilful practitioner. With equal zeal and thoroughness he studied the art of shoeing horses. Suffice it here to say that he succeeded finally, through the aid of influential friends, in having veterinary schools established by the Government throughout France. At first, Bourgelat was made the Director General of these schools, but later (1762) he was also appointed superintendent of the French breeding studs. He died, at the age of sixty-seven, on January 3, 1779.

Dezeimeris ("Dict. Hist. de la Méd.") and the writer of the article on Veterinary Science in the Encyclopædia Britannica are both agreed in ascribing to Bourgelat the credit of being the originator of veterinary schools. That his services were highly appreciated by men of science throughout Europe is shown by the facts that he was elected a member of the Paris Académie des Sciences and an associate member of the similar academy in Berlin.

Of his published writings the following deserve to receive special mention: "Eléments d'hippiatrique, on nouveaux principes sur la connaissance et sur la médecine des chevaux," Lyon, 1750–1753, 3 vols.; "Précis anatomique du corps du cheval, comparé à celui du boeuf et du mouton," fourth edition, Paris, 1807, 2 vols.; "Traité de la conformation extérieure du cheval; de sa beauté, de ses défauts; des considérations auxquelles il importe de s'arrêter dans le choix qu'on en doit faire; des soins qu'il exige, de sa multiplication, oudes haras, etc.," Paris, 1768–1769; "Essai théorique et pratique sur la ferrure, etc.," third edition, Paris, 1813; and "Essai sur les appareils et sur les bandages propres aux quadrupèdes," second edition, Paris, 1813 (with 21 plates).

A. H. B.

Bournemouth.—A city in England of 17,000 or more inhabitants, situated on the south coast of England, in Hampshire, thirty-seven and one-half miles from Southampton. "It is built on a flat, pine-covered heath which abuts abruptly on the sea in the form of great brown sandy cliffs." "The East Cliff, the West Cliff, the Valley, and the Coast are the four natural divisions of Bournemouth." The East Cliff, over a great part of its extent, slopes landward and thus has a westerly and southwesterly as well as a southerly aspect; it is the older residential quarter of Bournemouth. The West Cliff is more elevated and exposed than the East, and is the newer part of Bournemouth; it contains the larger number of boarding houses. The Valley of the Bourne affords the maximum of natural protection from the wind which the place can claim. The lower part is an attractive public garden, and the eastern slope, which is covered with

pines, affords a perfectly sheltered, sunny and quiet promenade and resting place; the well-known "Invalids' Walk" is to be found here. The coast is in the form of rugged high cliffs, bright with green and yellow gorse, and broken by deep irregular chines. Pines, much resembling those in our Southern States, are everywhere to be seen. On the East Cliff they are so abundant, fringing the streets and level walks and sheltering the houses, "that this portion of the city has been well described as a town in the wood." The heath all around Bournemouth is also covered with pine woods. The aromatic emanations from the pines are supposed to impart salubrious properties to the atmosphere. Beneath and about the pine trees the furze, rhododendron, and holly flourish in great luxuriance.

The sea lies full to the south, and on the eastern horizon are the Needles and Alum Bay, in the Isle of Wight. A pier 838 feet long extends into the sea and has specially constructed shelters for invalids. The soil, consisting of a greenish sand, is highly absorbent and very dry.

The principal facts relating to the meteorology of Bournemouth are exhibited in the following table:

Meteorological Means for Ten Years, 1881–1890.

	Jan.	Feb.	Mar.	April	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Year.
Mean temperature Fahrenheit at 9 A.M.	40.30°	40.70°	42.80°	49.80°	56.10°	61.50°	64.80°	63.60°	58.80°	51.00°	46.30°	41.00°	51.40°
Mean minimum temperature	34.40	34.50	34.90	38.50	44.60	50.30	54.20	52.60	49.70	42.90	39.80	34.60	42.60
Mean maximum temperature	44.70	45.80	48.50	44.90	62.00	68.20	71.00	70.90	65.80	56.30	51.00	45.00	57.10
Mean relative humidity	85.00	89.00	80.00	68.00	69.00	69.00	69.00	70.00	81.00	81.00	87.00	85.00	77.70
Mean rainfall	2.47	1.85	1.83	1.61	2.13	1.17	2.07	1.84	2.46	3.14	3.36	2.53	27.26
Mean number of rainy days	14.30	10.50	11.50	8.70	10.30	11.30	14.30	15.00	11.50	18.80	17.20	14.70	158.30

From the above we see that the mean temperature for the whole year is 49.7° F., or, at 9 A. M., 51.4° F. The mean minimum temperature is 42.6° F. and the mean maximum 57.1° F. The daily range of temperature is comparatively high. In January it is 10.3°, in July 16.8°. The mean relative humidity at 9 A. M. is 77.7, the lowest recorded in England. The mean total rainfall is 27.26 inches, and the mean number of rainy days 158.3. On an average it has been estimated that there are about two days a week during the winter season when patients cannot go out safely in consequence of rain or occasional cold winds or dust. The town possesses a good drainage system, and the water supply is above suspicion.

The general opinion of local practitioners, as expressed broadly, is that "most cases of pulmonary tuberculosis improve at Bournemouth." At the same time the climate of Bournemouth cannot be represented as equal to the best of the foreign climates, such as the Riviera or the Alpine stations. Dr. C. Theodore Williams' results are: "Twenty patients, each one winter at Bournemouth; six much improved, seven improved, two stationary, and five worse."

The special features of Bournemouth as a health resort, as summarized by the report of a committee of the Royal Medical and Chirurgical Society of London, 1895, to which the writer is indebted for the above account, are as follows:

"Bournemouth is distinguished by the general beauty of its position, which combines the attractions as well as the wholesome influences of sea and heath. As a whole, compared with England, it possesses a mild, bright, and fairly dry climate. The atmosphere is naturally pure, sunny, free from fog, redolent of the pine, of low relative humidity, and comparatively undisturbed by high or cold winds. The soil is dry and warm, permitting patients to sit with comparative safety in the open air; and it supports an abundant and luxuriant growth of non-deciduous trees and shrubs. The town area is very large in relation to the number of houses and inhabitants." On the other hand, "like other places on the south coast, it is subject to frequent and uncertain spells of bad weather, in the form of wet, cold, or both combined, and to even more dangerous, because deceptive, visitations of high east winds in the early spring."

"The kinds of cases which have been benefited by a residence at Bournemouth are chiefly as follows:

"(1) Cases of pulmonary tuberculosis which would do well at any good health resort. (2) Pulmonary tuberculosis in the incipient stage. (3) Quiescent pulmonary tuberculosis when the patient can spend a number of hours continuously in the open air. (4) Patients in the last stage of phthisis often enjoy an extension of life here. In general, cases that can take advantage of outdoor life do well, while those who are confined to the house do badly. (5) Chronic bronchitis without fever, and particularly recurrent bronchial catarrh with a moderate amount of expectoration, asthma, whether neurotic or catarrhal, the different parts of the town being tried if necessary. (6) Chronic Bright's disease, particularly of inflammatory origin. (7) The subjects of chronic malaria. (8) Sufferers from chronic gastric catarrh with emaciation. (9) The victims of nervous overwork, particularly with insomnia, provided they do not settle too close to the sea. (10) Delicate persons generally, including more especially elderly and aged people, and feeble and rickety children."

"The cases, on the other hand, which do not do well or even badly, are: (1) Persons confined to the house, applying chiefly to consumptives. (2) The subjects of pulmonary tuberculosis in its active stage, especially when attended with much fever and profuse expectoration. (3) Those suffering with dry irritable catarrh of the larynx and bronchi. (4) Sufferers from neuralgia."

The accommodations are good and abundant and of every variety. From a personal visit the writer was impressed with the beauty of the place, its clear, bright atmosphere, the abundant sunshine, its luxuriant vegetation, and the striking effect of the great number of pines everywhere. The sea view from the cliffs is most attractive, and there are many pleasing excursions inland over the thickly wooded heath. For an outdoor life one can hardly imagine a more attractive place of residence.

Edward O. Otis.

Bovell, James.—Born at Barbados, West Indies, in June, 1817. He studied medicine in London, Edinburgh, and Dublin, and after receiving his doctor's degree he returned to Barbados and commenced the practice of his profession. In 1848 he went to Canada and settled in the city of Toronto. In 1850 he took part in establishing the Medical Faculty of

Trinity College, in which he held the professorship of the Institutes of Medicine and at the same time was Dean of the Faculty. In conjunction with others, in 1851, he assisted in founding the *Upper Canada Medical Journal*, the first issued in the Province. Upon the disruption of the Medical Faculty of Trinity College, not long afterward, Dr. Bovell joined the Toronto School of Medicine, and delivered lectures on physiology and pathology during his connection with that institution. In 1870 the Bishop of Antigua, British West Indies, recognizing the fact that the doctor possessed qualities which admirably fitted him for missionary work—high attainments not only in general science but also in theology, united with a character of unusual devoutness—urged upon him the duty of taking Holy Orders. With many misgivings Dr. Bovell consented to do so, and thereupon gave up his official position in the medical school. He died at Nevis in the West Indies on January 6, 1880.

His contributions to periodical medical literature were numerous, and he was also a valued member of the Canadian Institute. (From data kindly furnished by Dr. A. Primrose of Toronto.) A. H. B.

Bowden Lithia Springs.—Douglas County, Georgia.

Post-office.—Lithia Springs. The Sweetwater Park Hotel was burned in January, 1912.

Access.—Viâ the Southern Railroad. These springs are located in Douglas County, 17 miles west of Atlanta, 300 miles distant from the Atlantic coast and at an altitude of 1,200 feet above the sea level. The surrounding country is of a somewhat rugged, broken character, interspersed with forests of pine, oak, maple, and cypress and watered by streams skirted by haw and holly. The temperature rarely reaches 90° F. in summer or extends below 40° above zero in winter, while the nights are proverbially pleasant. The surroundings of the place are exceptionally charming, the Shoals, the Ruined Mill, Chapel Hill, and the Dome Rock, showing the mighty action of some great sea in prehistoric times, the Mill in the Glen, the Old Distillery, and the Sweetwater Creek being also among the numerous features of interest. While people have resorted to these springs for about sixty years, only recently have they become very extensively known.

The use of the Bowden lithia waters is particularly recommended in various diseases of the digestive organs, in liver, kidney, and bladder affections, calculi, gravel, cystitis, and in gout and rheumatism. The external use of the water in bathing, for which there are excellent facilities, is said to be beneficial in skin affections, chronic ulcers, and glandular enlargements. The waters are used commercially, and may be found in most of the principal cities of the East and South.

Following are analyses of the waters:

One United States Gallon Contains:

Solids.	(Upper Spring.) Pratt, 1887.	(Lower Spring.) Pratt, 1889.	Doremus, 1890.
	Grains.	Grains.	Grains.
Carbonic acid as bicarbonates.	9.85		9.91
Lithium bicarbonate	2.85	1.67	4.45
Potassium bromide		5.29	
Potassium sulphate			1.73
Potassium bicarbonate	3.36		
Magnesium bromide	1.69	15.23	1.47
Magnesium bicarbonate	10.32		
Magnesium sulphate	4.41		
Magnesium iodide (iodine)	Traces.	.73	Traces.
Calcium bicarbonate	14.18		17.25

One United States Gallon Contains—*Continued*

Solids.	(Upper Spring.) Pratt, 1887.	(Lower Spring.) Pratt, 1889.	Doremus, 1890.
	Grains.	Grains.	Grains.
Calcium sulphate		20.21	12.15
Calcium phosphate	.61		
Strontium sulphate	1.02	.28	1.22
Ferrous bicarbonate	.21		.21
Sodium sulphate	16.25		8.03
Sodium chloride	133.71	124.49	121.78
Sodium phosphate		.89	
Aluminum sulphate	1.33	2.61	.53
Silicic acid (soluble)	1.12	1.96	1.26
Boric acid			Traces.
Manganese	Traces.		Traces.
Phosphoric acid			
Rubidium (spectroscopic analysis).	Traces.		
Fluorine	Traces.		
Loss on ignition			5.75
Total.	200.94	173.36	185.74

Emma E. Walker.

Bowditch, Henry I.—Born August 9, 1808, in Salem, Massachusetts. His father was Nathaniel Bowditch, the eminent mathematician. He received his degree of Doctor of Medicine from the Harvard Medical School in 1832, and then went to Paris, France, to complete his medical education. He remained in that city two years, and upon his return to this country in 1834 he established himself in practice in Boston. In 1846, when the visiting medical staff of the Massachusetts General Hospital was augmented from three to six, the new appointments were given to Drs. John D. Fisher, Oliver Wendell Holmes, and Henry I. Bowditch. In 1859 Dr. Bowditch was appointed to the Jackson Professorship of Clinical Medicine in the Harvard Medical School; his predecessor, Dr. George C. Shattuck, having been transferred to the Hersey Professorship of the Theory and Practice of Medicine. In the later years of his career Bowditch devoted himself largely to thoracic diseases; and at the same time he took an increasingly active part in the subject of Public Hygiene. Thoracic aspiration, an operation frequently if not commonly credited to the French physician Dieulafoy, was performed and strongly advocated by Dr. Bowditch several years before the latter published his method. Dr. Bowditch performed the operation of thoracocentesis by means of an exploring trocar and a suction pump. His death occurred on January 14, 1892.

Dr. Bowditch was a frequent contributor to current medical literature. In 1848 he published "The Young Stethoscopist." The first one of his communications on "Paracentesis Thoracis" appeared in 1851. In 1862 he published his exhaustive investigations on soil moisture as a cause of pulmonary consumption in Massachusetts. He also translated Louis' "Researches on Phthisis," his "Memoirs on Clinical Instruction," and his "Observations on Gastroenteritis." A. H. B.

Bow Leg.—*Synonym:* Genu Varum.

In the popular sense bow leg includes the deformities which cause separation of the knees when the ankles are in contact with each other; but, strictly speaking, bow leg implies an outward bending of the tibia and fibula, and genu varum a deformity in which the greatest distortion is at the knee, in which the femur is involved, the opposite of genu valgum. In most instances simple bow leg is associated with

FIG. 851.—Bow Legs of the Genu Varum Type.

genu varum, and genu varum with a certain degree of bending of the bones of the leg, so that the two terms are properly synonymous.

ETIOLOGY. — Bow leg is the most common of the distortions of the bones, constituting about ten per cent. of the cases treated in orthopedic clinics. It is essentially a deformity of childhood. It may be congenital, and it is not uncommon in vigorous infants who stand at an early age. But in most instances it is an effect of rachitis, often of a mild type, and it develops therefore soon after the child begins to walk, although the tendency to deformity may have been acquired before this time. The deformity sometimes increases during adolescence and it may be acquired in later life, as an effect of occupation, or injury or disease, but these types are comparatively uncommon.

SYMPTOMS. — The essential symptom of bow legs is the deformity. In the genu varum type, the femur is abducted and rotated outward while the tibia is rotated inward; and in simple bow leg there may be a spiral inward twist of the tibia, so that intoeing, "pigeon toe," may be one of the effects of the deformity.

In the more extreme cases, in which there is laxity of the ligaments at the knee-joint and in the progressive type of adolescence, the patient may suffer from pain and weakness at the knee-joint, but ordinarily discomfort is not a symptom.

TREATMENT.—There is a strong tendency toward spontaneous recovery, the "outgrowth" of deformity. But although the distortion may be entirely cured by the natural process, it is far more often simply modified and made less noticeable. This may be inferred from the fact that bow leg in the slighter degree is so common in later life. According to the writer's observations, about one adult male in five has noticeable deformity of this character, a proportion that is apparently not exceeded among children. Thus, although bow leg may cause no physical discomfort, it is, from the esthetic standpoint, of sufficient importance to merit treatment in all cases.

It may be easily overcome in infancy by systematic manual correction. It may be prevented in rachitic children by the avoidance of attitudes that induce the deformity, especially standing when the bones are weak. In the slight degree of deformity in walking children, the tendency toward distortion may be counteracted somewhat by making the sole of the shoe slightly thicker on the outer border. If the deformity is more marked, or if it is increasing, or if the bones are abnormally flexible, a brace should be applied. This consists essentially of a light bar of steel, reaching from the internal condyle of the femur to the sole of the shoe. This is suitably padded at the points of pressure and is provided with a laced band which is passed around the limb at the point of greatest deformity, thus supporting it and exercising slight corrective force. If the distortion is most marked at the knee, the bar should be prolonged to the upper third of the thigh, and a second band should be applied about the knee. A jointed brace is less effective than is the simple form that has been described.

FIG. 852.—Bow Legs in which the Principal Distortion is Below the Knees.

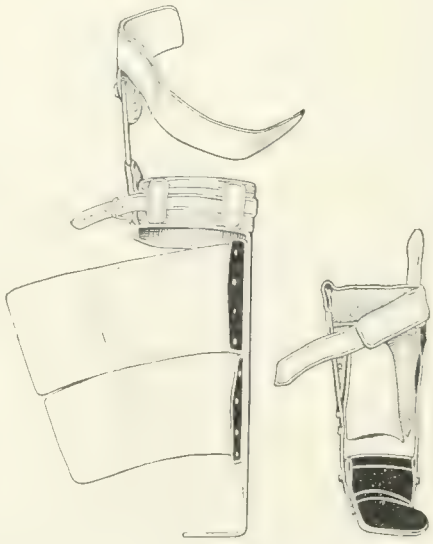

FIG. 853.—The Long and the Short Bow-leg Brace.

The function of a brace is principally support. The correction of the deformity may be hastened by daily systematic manual straightening, and cure is accomplished by the natural transformation of the internal structure of the deformed part which begins when the static conditions are changed. In older subjects, when the bones are more unyielding, operative treatment is indicated.

Osteoclasis or osteotomy may be employed. As a rule it is sufficient to straighten the tibia at the point of greatest deformity, but in exceptional cases both the tibia and femur may require

treatment. By far the most satisfactory method is partial osteotomy, combined with forcible correction. A small sharp osteotome is inserted directly over the point of greatest deformity on the concave side of the tibia, and when the cortex on its inner surface has been divided the fracture is completed by manual force. The fibula may be bent or broken as it is more or less resistant. In all cases the distortion should be slightly overcorrected, and the limb fixed in this position until union is complete.

Other Varieties of Deformity.—Bow leg may be unilateral, or it may be combined with knock-knee.

Anterior Bow Leg.—Anterior bow leg is a deformity in which the tibia is bowed forward. Its antero-posterior diameter is increased, the crest is prominent and projects sharply beneath the skin. This distortion is usually symptomatic of pronounced rachitis; it is often combined with knock-knee, or with general distortions of the limbs, "corkscrew" deformity. As the weight is thrown upon the anterior part of the foot, the heel projects and the gait is awkward and shuffling. The distortion is not usually amenable to treatment by braces, and osteotomy is indicated. In the more extreme cases in which the tissues on the posterior aspect of the leg are shortened, division of the tendo Achillis is required to permit correction.

ROYAL WHITMAN.

Bowman, William.—Born at Nantwich, Cheshire, England, on July 20, 1816. He obtained his first medical training in the Birmingham General Hospital, and then visited Dublin, Leyden, Amsterdam, Bonn, Heidelberg, Munich, Vienna, Berlin, etc., in search of further knowledge. In 1838 he obtained the position of Demonstrator of Anatomy and Curator of the Anatomical Museum in London. In 1846 he was given the position of Assistant Surgeon at the London Ophthalmic Hospital, Moorfields, and in 1854 that of full surgeon. In 1877 he was made Consulting Surgeon of the same institution. After 1860 honors of all sorts were literally showered upon Dr. Bowman, who by this time had attained great celebrity both as an ophthalmologist and as an authority in microscopic anatomy. Among other things he was made a baronet. He died on March 29, 1892.

Of his published writings on topics belonging to the domain of ophthalmology the following deserve to be mentioned: "On some Points in the Anatomy of the Eye, chiefly with reference to its Powers of Adjustment," British Association Report, 1847; "Observations on the Structure of the Vitreous Humor," Dublin Quarterly Journal of Med. Science, vi, 1848; and "Lectures on the Parts concerned in the Operations on the Eye," London, 1849.

A. H. B.

Box.—*Buxus.* The leafy twigs of *Buxus sempervirens* L. (fam. *Buxaceæ*), a slow-growing evergreen shrub, of the southern part of Europe and the East, frequently cultivated for ornament, were formerly much used as a febrifuge, tonic, and antiperiodic.

The bitterness of box is due to the alkaloid *buxine*, identical with berberine, already considered under "Bibiru Bark." A second alkaloid, *parabuxin*, was found by Pavia to accompany the buxine in box; and it is still probable that some other principle may be found to explain the poisonous qualities it has been occasionally observed to have. Box has had some reputation as a febrifuge and tonic; in large doses it is purgative and emetic. It is suspected of being sometimes used to replace hops in beer. It is little employed in medicine to-day, in doses of one to two drams. Buxine sulphate has been used as a tonic in doses of one to two grains; as a febrifuge, eight or ten times as much, gr. viij.–xv. (0.5–1.0).

H. H. RUSBY.

Bozeman, Nathan.—Born in Butler County, Alabama, March 26, 1825. He took his degree of Doctor of Medicine at the University of Louisville, Kentucky, in 1847. From 1849 to 1858 he practised his profession in Montgomery, Alabama, a small portion of the time in partnership with Dr. J. Marion Sims. Although he devoted himself mainly to gynecological work, he occasionally performed surgical operations of a different nature. Thus, in 1854, he successfully removed (the operation had been performed only once before in the United States) an elephantiasis of the scrotum weighing forty-six pounds. Later in the same year he performed for the first time, and according to the method which he himself devised, the operation for curing a vesicovaginal fistula combined with a tear of the cervix uteri. In 1856 he operated successfully on a vesicouterine fistula, and in 1857 on a vesico-uterovaginal fistula. In 1858 he made a trip to Europe and demonstrated his method of operating in the hospitals of London, Edinburgh, Glasgow, and Paris. In 1870 and 1871 he perfected his operations for the cure of urethrovaginal and recto-uterovaginal fistulæ. In 1874 he visited Germany and demonstrated his operative methods, first in Heidelberg in that year, and then in Vienna in 1875. In 1876 he made similar demonstrations in the Hôpital Beaujon in Paris. Upon his return to New York in 1877 he resumed the practice of his profession in that city. His death occurred December 16, 1905.

A. H. B.

Bradford Mineral Springs.—Merrimac County, N. H.

POST-OFFICE.—East Washington. Hotel.

ACCESS.—A stage runs daily from Hillsboro, N. H., to the springs. The Springs are one mile from East Washington Post-office.

This spring became known to the white settlers in 1770, and since early in the present century its waters have been used for medicinal purposes. An analysis by Dr. Jackson of Boston, subsequently confirmed by Dr. Richards of Poughkeepsie, New York, showed the presence of the following ingredients: Sodium chloride, potassium chloride, sodium carbonate, calcium carbonate, magnesium carbonate, calcium phosphate, iron oxide, aluminum oxide, organic matter, sulphur, carbonic acid gas.

We are unable from this analysis to assign the water to its proper class, although it is probably a sulphureted chalybeate. The spring yields twenty-one hundred gallons hourly. The water is clear and sparkling, and emits an odor of sulphureted hydrogen gas. It has been successfully used by the residents of the neighborhood in the treatment of certain cutaneous diseases, especially eczema. It is said to be a very efficient diuretic and tonic, and seems to be well adapted for rheumatism and diseases of the alimentary tract, and for conditions in which the urine is scanty and high-colored. As a douche in nasal catarrh and in catarrhal states of the vagina and uterus it has been found useful. There are bathing facilities for guests who wish to take hot or cold sulphur baths. The surroundings of the place are very attractive, and ample amusements and diversion are afforded the visitor in the way of bowling, shooting, fishing, driving, etc.

Bradycardia.—See *Arrhythmia, Cardiac.*

Braid, James.—Born in Fifeshire, Scotland, in 1795. He practised for some years in Leads Hill, Lanarkshire, England, and then settled in Manchester, where, in 1841, he accidentally made the discovery that a person may, by looking intently for a certain length of time at a glittering object, pass into that condition of nervous sleep to which the name "hypnotism" has been given. Durand de Gros, who devoted

considerable study to the phenomenon, was the first to apply to it the name "Braidism." Braid's death occurred March 25, 1860.

Of the articles published by Braid in relation to hypnotism, the more important ones are the following: "Neurypnology; or the Rationale of Nervous Sleep, considered in relation with Animal Magnetism, etc.," London, 1843; "Magic, Witchcraft, Animal Magnetism, Hypnotism and Electrobiology," London, third edition, 1852; "Hypnotic Therapeutics, Illustrated by Cases," Monthly Journal, 1853. A. H. B.

Brain, Abscess of.—See *Encephalitis.*

Brain, Anatomy of the.—Structural Elements.—The external configuration of the brain has been shaped by the development of internal centers of correlation whose size, position, and fiber connections are determined by the functional needs of the body. Each of these centers necessarily differs from all of the others in respect of the details of internal organization and type of associational connection with other centers. Accordingly, the consideration of the gross and microscopic anatomy of the central nervous system should go hand-in-hand.

In the nervous system, as in other parts of the body, the cell is commonly regarded as the anatomical unit. This unit is termed the neurone and comprises the cell nucleus, its immediately surrounding protoplasm and the outlying fibrous processes connected therewith. In some of the peripheral diffuse sympathetic ganglionic plexuses these processes appear to be united into a true syncytial network, with little functional differentiation among the nerve fibers. But in the cerebrospinal nervous system each neurone exhibits a functional polarization, such that some of its processes, the dendrites, are adapted for conducting incoming (cellulipetal) impulses, while one process (sometimes more than one), the axone (neurite or axis cylinder process), conducts only in the efferent or cellulifugal direction (Fig. 854). The axone (and, in the case of the neurones of the root ganglia of the cerebrospinal nerves, the dendrite also) may be surrounded by a special fatty sheath of myelin, the medullary sheath.

The dendrites are usually relatively short, thorny, and freely branched. The axone, on the other hand, is slender and smooth; it may be very long, as in the type I neurones of Golgi (Fig. 856), or it may break up in the immediate neighborhood of the cell body into a diffusely branched ending, as in Golgi's type II (Fig. 857).

The point where the axone of one neurone comes into physiological relation with another neurone is known as the synapse. Its precise nature is still obscure, but it is known that a delay in conduction occurs at this point and also that the irreversible character of the nervous impulse is due to the fact that these impulses can pass the synapse in only one direction. Probably the synapse is from the functional standpoint the most important element in the nervous system. The synapse usually exhibits a dense interlacing of the terminal arborization of an axone of one neurone with the bushy dendrite of a second neurone. In other cases the terminal arborization takes the form of a delicate network which twines around the cell body of the neurone of the second order or of a calyx-like expansion or coarse-meshed reticulum closely enveloping the cell body. Various types of synapse are illustrated in Figs. 858, 859, 860, 861, and 972.

The axone may branch before the terminal arborization is reached, thus coming into relation with the dendrites of two or more widely separated and physiologically diverse neurones of the second order; or two or more dendrites of a neurone of the second order may enter into synaptic relation with neurones of the first order belonging to different physiological systems. This is the mechanism of correlation. The condition illustrated in Fig. 860 provides one method by which a neurone may discharge its impulse into a large number of neurones of the same physiological system, thus providing for a great increase in the total amount of nervous energy liberated by a given stimulus. Many different forms of such "avalanche conduction" (Ramón y Cajal) are found in the central nervous system.

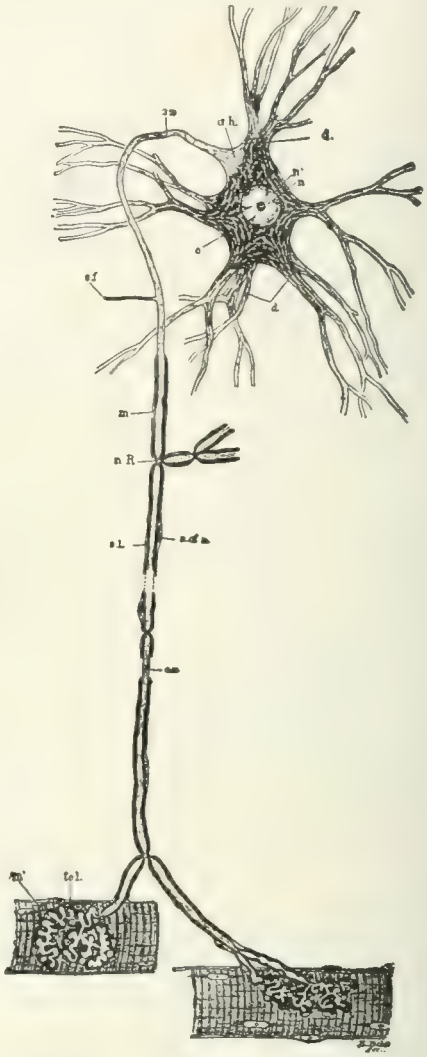

Fig. 854.—Schematic Representation of a Lower Motor Neurone. The motor cell from the ventral horn of the spinal cord, together with all its protoplasmic processes and their divisions, its axis-cylinder process with its divisions, side fibrils, or collaterals, and terminal ramifications (motor end-plates) in the muscle, represent parts of a single cell or *neurone*. *a.h*, Axone hillock devoid of Nissl bodies, and showing a tendency to fibrillation; *a.x*, axis cylinder or axone, also indistinctly fibrillated. This process, at a short distance from the cell body, becomes surrounded by a myelin sheath, *m*, and a cellular sheath, the neurilemma, the latter not being an integral part of the neurone; *c*, cytoplasm showing the dark-colored Nissl bodies and lighter ground substance; *d*, protoplasmic processes (dendrites) containing Nissl bodies; *n*, nucleus; *n'*, nucleolus; *n.R*, node of Ranvier; *sf*, side fibril; *n of n*, nucleus of neurilemma sheath; *tel.*, motor end-plate; *m'*, striped muscle fiber; *s.L.*, segmentation of Lantermann. (From "The Nervous System and Its Constituent Neurones," D. Appleton & Co., New York, 1899.)

The structural peculiarities of the cerebrospinal neurones are of two chief kinds. In the first place, the outgrowth of fibrous processes, highly differentiated for the conduction of nerve impulses for long

distances, facilitates the coordination and integration of all bodily activities; and, in the second place, within the body of the neurone there is a highly specialized substance allied to the nucleoproteins, the chromophilic substance or Nissl bodies (Figs. 855, 871), which seems in some way to be associated with the special metabolism of the neurone.

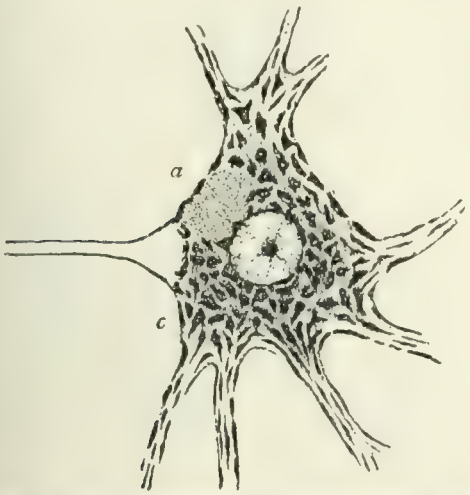

Fig. 855.—The Cell Body from a Neurone Similar to that of Fig. 854, from the Spinal Cord of an Ox, stained by Nissl's Method to Show the Chromophilic Bodies. *a*, Pigment; *b*, axone; *c*, axone hillock; *d*, dendrites. (From Barker, after von Lenhossék.)

Fig. 856.—Pyramidal Cell of Golgi's Type I from the Human Cerebral Cortex, Prepared by Golgi's Bichloride of Mercury Method. *a*, Cell body; *b*, apical dendrite; *c*, lateral dendrites; *d*, axone with collateral branches. Only a small part of the axone is included in the drawing. (After O. S. Strong, from Bailey's Histology.)

The Nissl bodies are absent in some very small neurones which have scanty cytoplasm and very short axones, such as the granules of the cerebellum (Fig. 862), olfactory bulb and retina. In other neurones, the somatochromes, the chromophilic substance is arranged in more or less definite masses scattered throughout the cytoplasm. This substance had been

Fig. 857.—Cell of Golgi's Type II from the Cerebral Cortex of a Cat. *a*, Axone, which is seen to break up into a rich plexus of terminal fibers near its origin; *x*, the coarser dendrites. Practically the entire neurone is included in the drawing. (After Kölliker, from Bailey's Histology.)

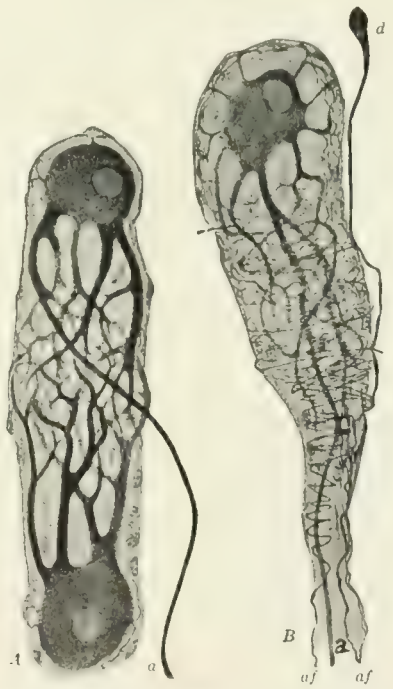

Fig. 858.—Sympathetic Nerve Cells and Their Capsules. *A*, Two-celled glomerulus; *B*, cell surrounded with the pericellular terminal arborizations of two fibers (*a.f.*) passing to the cell and forming a spiral synapse; *a*, axon of the cell shown; *d*, fiber, probably dendritic, with bulbous termination. Cajal's silver stain. (After Ramón y Cajal, from Bailey's Histology.)

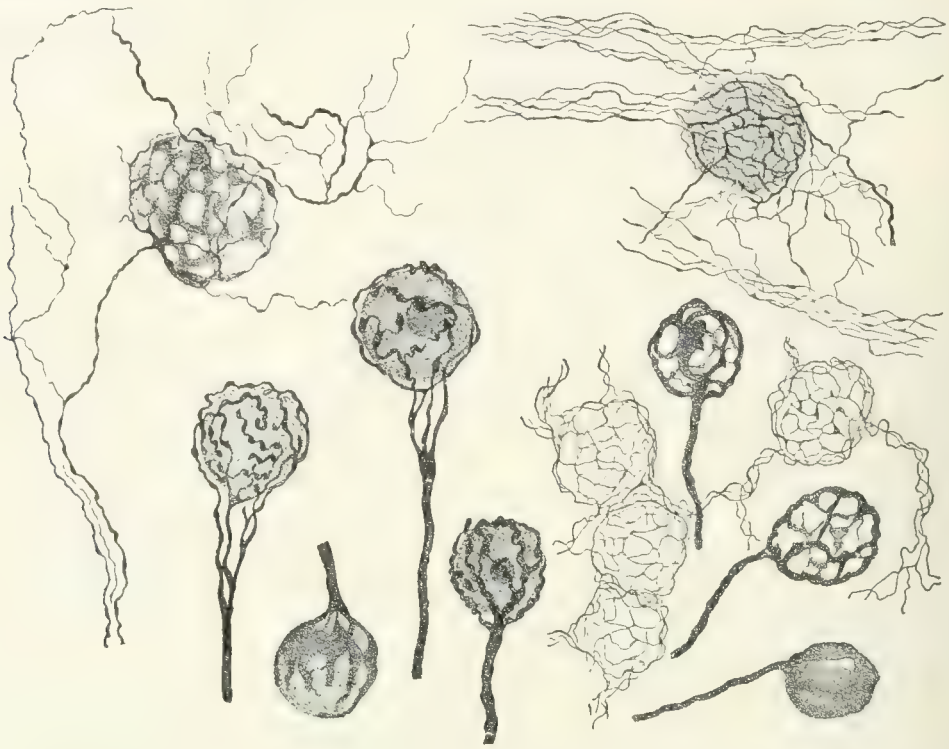

FIG. 859.—Neurones from the Corpus Trapezoideum of a Cat, to Illustrate Different Forms of the Synapse. (From Edinger, after Veratti.)

shown to be related to the chromatin of the nucleus. It is comparable with the chromidial apparatus of other than nerve cells. The Nissl bodies are regarded by some neurologists as artifacts, though they can readily be stained by vital dyes. They are most clearly demonstrated by the special method of staining with methylene blue devised by Nissl, though they can be selectively stained by many other dyes.

The chromophilic substance exhibits characteristic differences in amount and arrangement in different types of neurones, the basis for which is obscure, but is undoubtedly connected with the specific function of the cell. This is shown by the fact that in preparations stained by Nissl's method the boundaries of different regions known on other grounds to have separate functional connections can usually be recognized, not only by the size and shape of their cell bodies, but also by the character of their Nissl substance. The form and size of the Nissl bodies are also very susceptible to changes in the metabolic state of the cell, as shown by studies on fatigue and various pathological processes. This fact is taken advantage of to determine experimentally the location of the cell bodies from which the fibers of any given nerve or tract arise. Thus, for instance, the exact sources within the brain of the motor fibers in any cranial nerve can be determined by experimental section of the root in question in an animal, followed within a few days by the death of the animal and a microscopical study of the brain by Nissl's method. The cell bodies whose axones were severed by the operation will be found in a state of chromatolysis, *i.e.* the Nissl bodies will be partially or completely dissolved (Fig. 863).

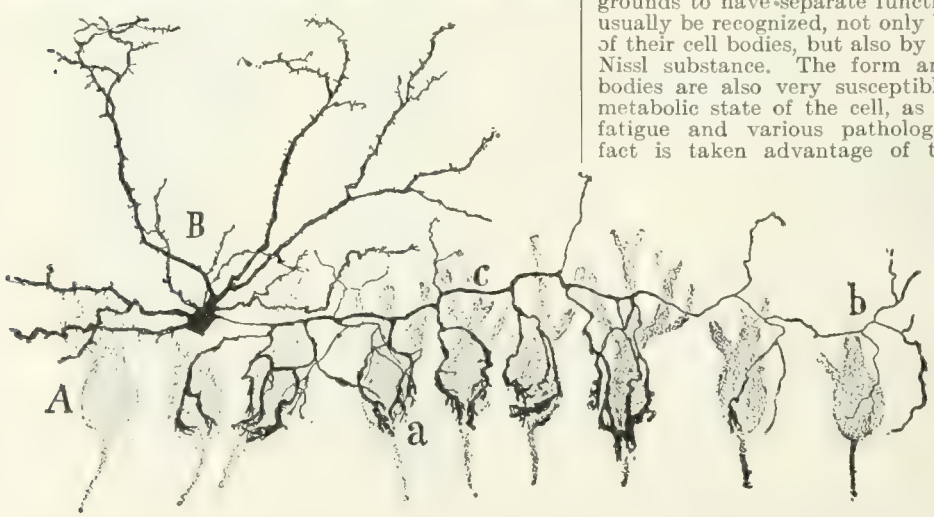

FIG. 860.—A "Basket Cell" from the Cerebellar Cortex of a Rat, Illustrating the Synaptic Discharge of a Single Neurone of the First Order Directly upon the Cell Bodies of many Neurones of the Second Order. *A*, Cells of Purkinje; *a*, the basket-like synapse on the body of a Purkinje cell; *B*, the basket cell; *b*, terminus of the axone; *c*, axone of basket cell. (After Ramón y Cajal; cf. Fig. 936.)

Another very characteristic structure in the cytoplasm of nerve cells is the neurofibrils. These deli-

cate, thread-like bodies have been described by Bethe, Apáthy and others, in certain invertebrates, as passing from one cell body to another through anastomosing nervous processes of the neuropil, and the same thing occurs in some peripheral nervous plexuses of vertebrates. But in the cerebrospinal nervous system such a connection between neurones is not evident and its presence is commonly denied. The neuro-

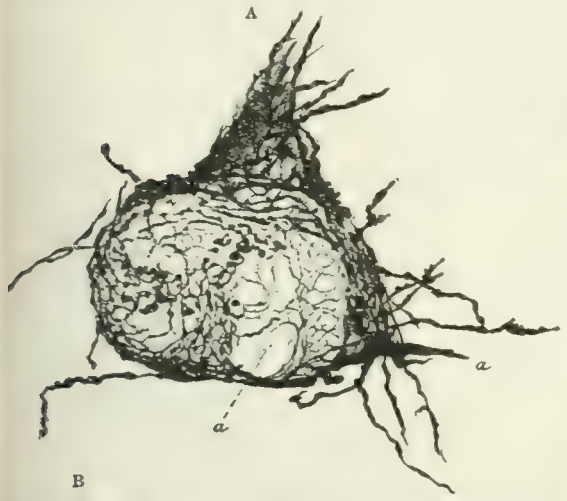

FIG. 861.—Cell from the Nucleus Cochlearis Ventralis of a Cat, stained by Golgi's Method. The cell body is surrounded by a pericellular network believed to represent the terminals of axones from other neurones. The network surrounds the whole cell and a dendrite passing upward. The fiber *a* corresponds to one of the thickened fibers of the nervus cochlearis described by Ramón y Cajal and Held. (After Held.)

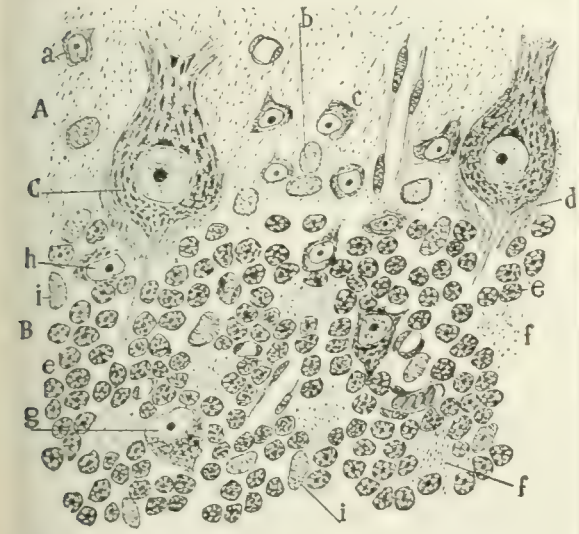

FIG. 862.—Vertical Section Through the Adult Human Cerebellar Cortex, stained by Nissl's Method; cf. Fig. 955. *A*, Inner part of the molecular layer; *a*, stellate cell; *B*, granular layer, showing only the nuclei of the granule cells, their cytoplasm containing no chromophilic substance; *b*, nuclei of the epithelial-like neuroglia cells (cells of the fibers of Bergmann); *C*, cytoplasm of a Purkinje cell, showing numerous chromophilic granules; *c*, stellate cell with marginal chromophilic substance; *d*, fibrillar substance corresponding to the basket-like synapse seen in Fig. 860; *e*, nuclei of the granule cells; *f*, islands or glomeruli in the granular layer; *g*,*h*, Golgi cells in the granular layer containing chromophilic granules; *i*, nuclei of neuroglia cells. (From Bailey's Histology, after Ramón y Cajal.)

fibrils are found in both dendrites and axones and usually pass through the cell body from one process to another (Figs. 864, 865, 868). The relations of neuro-fibrils to the fibrils developed in neuroglia, con-

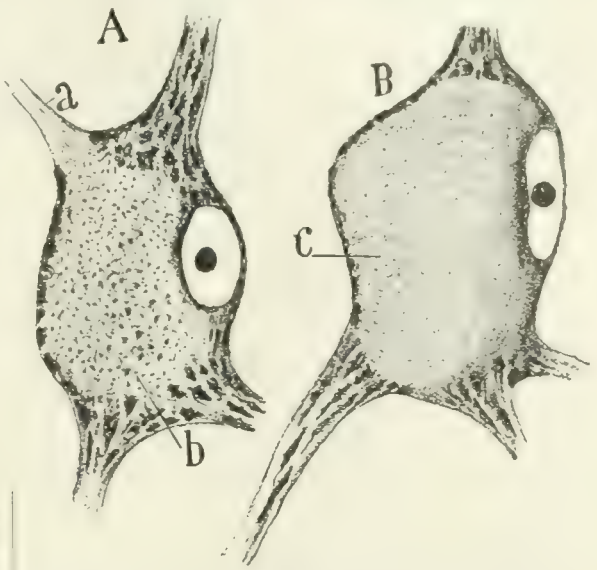

FIG. 863.—Two Motor Neurones from the Ventral Horn of the Thoracic Spinal Cord of a Rabbit, Fifteen Days after cutting the Major Sacro-Sciatic Nerve, to Illustrate the Chromatolysis of the Nissl Substance During the "Axonal Degeneration." *A*, Cell in which the chromophilic bodies are partially disintegrated (at *b*) and the nucleus eccentric; *B*, cell showing more advanced chromatolysis (*c*), the chromophilic substance being present only in the dendrites and around the nucleus in the form of a homogeneous mass; *a*, axone. (After Strong, from Bailey's Histology.)

nective tissue and other non-nervous cells is not clear. The wide-spread belief that the neurofibrils constitute the essential conducting elements is not universally accepted. In the developing embryo the functional activity of the nerves precedes the appearance within them of any demonstrable neurofibrils.

Numerous minute highly refractive granules, canals of various shapes and frequently pigment and other inclusions occur in the cytoplasm in the spaces between the Nissl bodies and neurofibrils. All of these structures are embedded in a clear fluid ground substance, the functional significance of which is unknown. The granules are known to be of two sorts (Cowdry, 1912): (1) the granules of irregular size and shape demonstrated by the erythrosin-methylene blue method of Held and especially abundant in the axone hillock, called type I by Cowdry (Fig. 867), and (2) more regular, uniformly distributed rod-like granules, type II of Cowdry, which agree in every respect with the mitochondria of the general cytologists (Fig. 866). The canalicular apparatus assumes exceedingly varied forms (Fig. 869) and has often been confused with other structures. It is the same as the clear intracellular canals of von Bergen, Bensley and others, the spiremes of Nelis, the Binnennetz of Kopsch, the Saftkanälchen of Holmgren, and probably the endocellular network of Golgi (Fig. 870).

The most diverse views have been expressed regarding the significance and relationships of the Nissl bodies, mitochondria and other cytoplasmic granules, neurofibrils and canalicular apparatus. That these are distinct elements in the adult neurone has been shown by Cowdry, who succeeded in demonstrating them all at the same time in a single nerve cell. Figs. 866 to 869 are drawn to a uniform scale from some of his preparations of spinal ganglion cells,

and illustrate typical forms assumed by these cytological elements when specifically stained.

The nucleus of nerve cells, as compared with that of most other cells in the body, is relatively large but poor in chromatin or other basophile substance. Most of the chromatin is usually aggregated into a dense globular mass, or false nucleolus (Figs. 855, 866, 871). There is in the nucleus also a true nucleolus which stains with acid dyes, and also a nucleoprotein which exhibits the acidophile reaction, the so-called oxychromatin of M. Haidenhain and Scott.

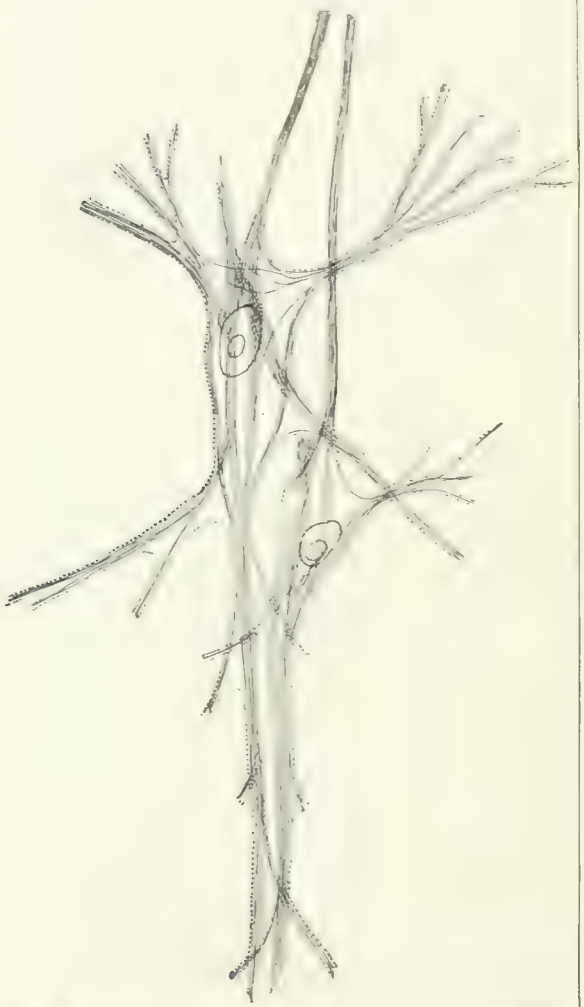

Fig. 864.—Neurofibrils in Pyramidal Cells of the Human Cerebral Cortex. (After Bethe, from van Gehuchten's Système Nerveux.)

Nerve cells often contain masses of pigment (cf. Fig. 855) and droplets of fatty or lipoid substances, the significance of which is as yet unknown.

The supporting elements of the brain bear some relation to the connective tissue cells and fibers, though they are, for the most part, developed, like the neurones, from the ectoderm rather than from the mesoderm. As will appear beyond, both the neurones and the neuroglia cells have a common origin from the epithelium of the primitive neural tube. The ependyma which lines the ventricles is derived directly from this primary epithelium and its internal limiting membrane. In the spinal cord and in some of the thinner parts of the brain the ependyma cells retain their continuity through the brain substance from the ventricular to the pial surface up to a late embryonic period (Fig. 881) or, as in the retina, even to adult life. But many of these cells become detached and develop into free glia cells. Other similar glia cells are said to be formed from the same germinative cells which give rise to neurones.

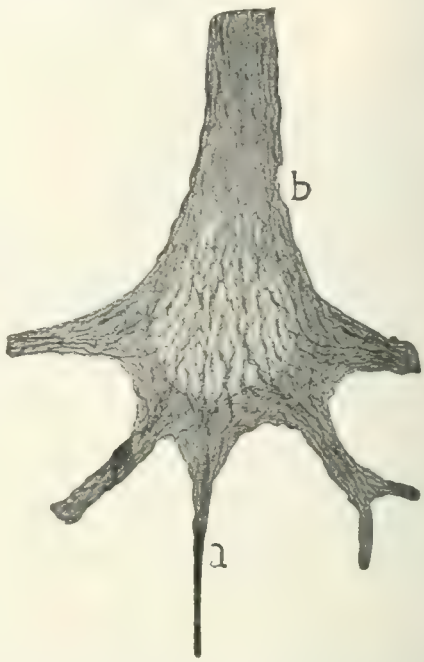

Fig. 865.—Large Pyramidal Cell from Cerebral Cortex of Cat, Illustrating the Arrangement of the Neurofibrils Stained by the Silver Reduction Method of Ramón y Cajal. *a*, Axone; *b*, main dendrite. (After Ramón y Cajal, from Bailey's Histology.)

The glia cells when treated by the Golgi process appear as small cell bodies with numerous slender radiating processes (Fig. 872); but when stained by the special methods devised by Weigert and others it is found that these processes are of two sorts. Some appear to be ordinary protoplasmic processes, while others are long slender fibers of a different chemical nature which pass through the cytoplasm

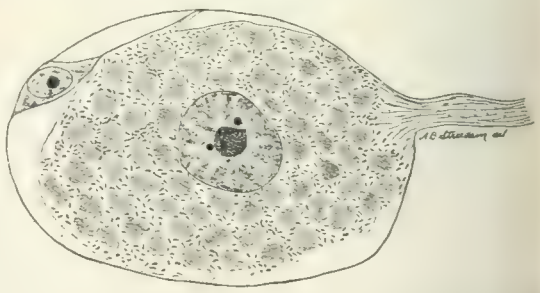

Fig. 866.—Section of a Pigeon's Spinal Ganglion Cell prepared by Bensley's (*Am. Jour. Anat.*, 1911, p. 309) Anilin Fuchsin-methyl Green Method. The mitochondria (neurosomes of type II) appear as minute rod-shaped bodies of uniform size distributed evenly throughout the cytoplasm; the Nissl bodies as larger, irregular, homogeneous granules of a lighter color. × 1066.

without apparent connection with it (Fig. 873). These neuroglia fibers are probably formed in earlier developmental stages much as connective tissue fibers are derived from connective tissue cells.

The neuroglia is commonly regarded as serving simply as a mechanical support for the nervous ele-

Fig. 867.—Section of a Pigeon's Spinal Ganglion Cell treated by Held's (*Archiv f. Anat. u. Phys.*, 1895, p. 399) Erythrosin-Methylene Blue Method. The neurosomes of Held (type I) appear as small particles of irregular size and shape, not distributed equally throughout the cytoplasm like the mitochondria, but aggregated in the region of the axone hillock. The Nissl bodies are larger, irregular and of a darker shade. × 1066.

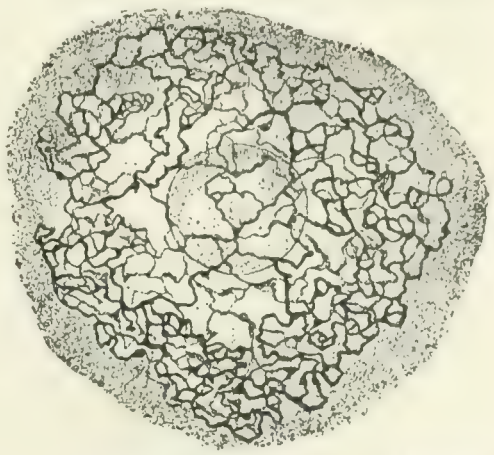

Fig. 870.—Spinal Ganglion Cell of a Dog exhibiting Golgi's Endocellular Network. (After Golgi, from van Gehuchten's Système Nerveux.)

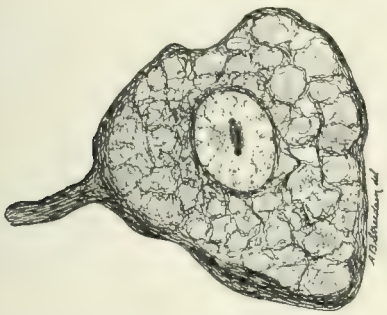

Fig. 868.—Section of a Pigeon's Spinal Ganglion Cell prepared by a Modification of Cajal's Silver Impregnation Method, toned with Gold and Counterstained with Toluidin Blue. The neurofibrils appear as black threads distributed between the lighter colored, homogeneous, flake-like Nissl bodies. × 1066.

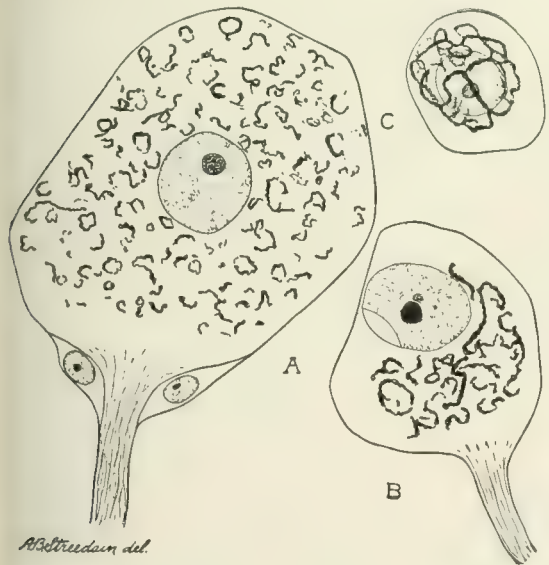

Fig. 869.—A Group of Pigeon's Spinal Ganglion Cells, seen in Section, prepared by Kopsch's Osmic Acid Method. Three different configurations of the canalicular apparatus are seen, namely: *A*, the diffuse, *B*, the circumscribed excentric, and *C*, the circumnuclear. × 1066.

ments. Some neurologists believe that it also serves as an insulating material between the neurones. Neuroglia cells, moreover, play an important part in the growth of certain tumors and in other pathological processes. The intimate relation of neuroglia to the blood-vessels has suggested that it also plays a part in the metabolism of the brain during normal function; but exact information regarding these supposed functions is still lacking (cf. Ramón y Cajal, 1909, pp. 246–252).

Technique.—The study of the nervous system may be conducted by the usual methods of anatomy and histology, but only small progress can be made

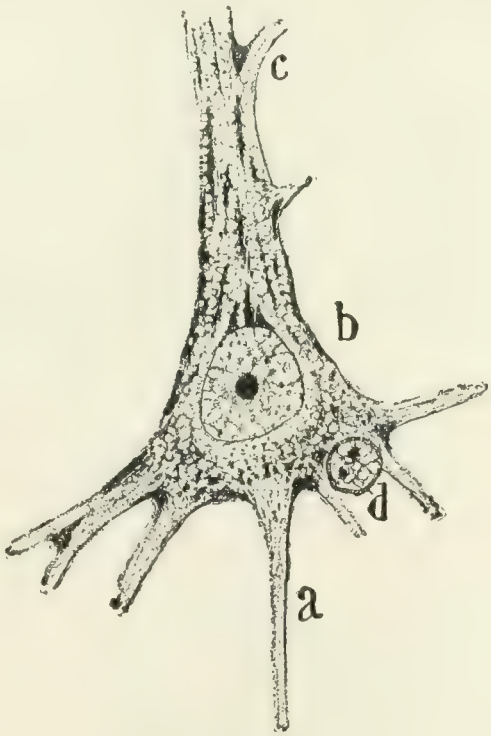

Fig. 871.—The Body of a Pyramidal Cell from the Cerebral Cortex, stained by Nissl's Method, Illustrating the Characteristics of the Chromophilic Substance and the Nucleus. (After Ramón y Cajal.)

without further recourse to many highly special neurological procedures. In the study of the gross structure of the brain the earlier anatomists obtained excellent results by teasing or tearing the tissue with blunt

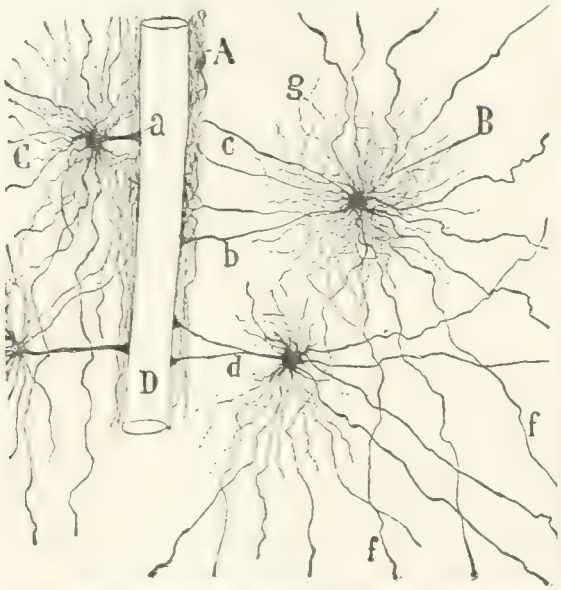

Fig. 872.—Glia Cells impregnated by the Golgi Method. (After Ramón y Cajal.)

instruments, a useful practice which has been too much neglected in favor of section pictures since the introduction of histological methods (see Curran, 1909, and the literature there cited). On the preservation of brains for anatomical and museum purposes, see Hrdlicka (1906).

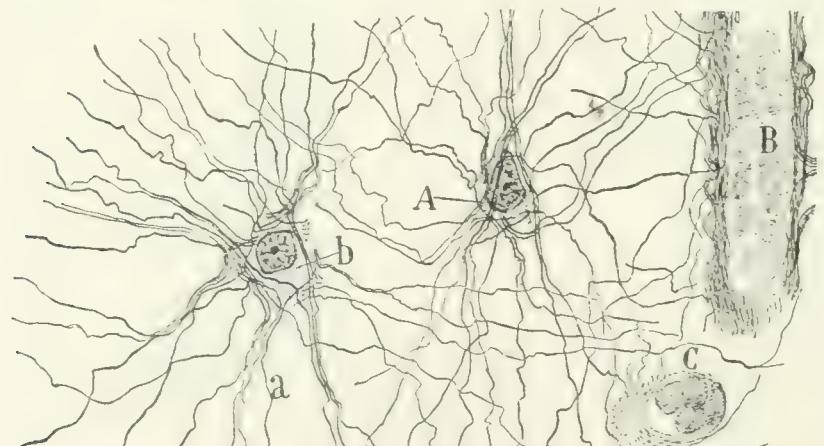

Fig. 873.—Neuroglia Cells and Fibers from the White Matter of the Human Cerebellum stained by Weigert's Neuroglia Stain. *A*, Neuroglia cell; *b*, its cytoplasm; *a*, neuroglia fibers; *B*, blood-vessel cut longitudinally, and *C* a vessel cut transversely, showing enveloping neuroglia fibers. (After Ramón y Cajal, from Barley's Histology.)

The histological methods which have been devised for various neurological purposes are much too numerous and too intricate even for summary in this place. See the works of Lee (1905), Hardesty (1902), Pollak (1905), the summary by Dr. Barker in vol. ii. of the second edition of this Handbook, pp. 325–331, articles in the *Zeitschrift f. wissensch. Microscopie* and the summaries in Merkel und Bonnet's Ergebnisse der Anatomie and other serials.

General Morphology and Embryology.—Preliminary to a consideration of the details of the anatomical structure of the brain, we shall in this section review some of the general morphological and physiological principles upon which that structure is elaborated. Most of these principles are best illustrated by a review of the embryological development of the nervous system; some are better revealed by selected illustrations taken from comparative anatomy; and many are shown most clearly by a comparison of the embryological stages with corresponding stages in the evolutionary or phylogenetic history of the vertebrate nervous system. While the embryological development of the human brain by no means gives us an accurate recapitulation of the phylogenetic history of this organ, nevertheless there are certain striking resemblances between definite stages of the developing brain and the adult or embryonic brains of lower vertebrates which illuminate many human structures whose significance would otherwise remain obscure and which suggest the broad lines of the probable phylogeny. Accordingly, we shall not hesitate in this and the following sections to make comparisons with the brains of lower vertebrates where important general principles can thus be illustrated.

The entire cerebrospinal nervous system of vertebrates is developed from the dorso-medial ectoderm of the embryo (Fig. 874). The same holds true for most, and probably all, of the sympathetic nervous system. The only important exception to this rule is the penetration into the brain and spinal cord in relatively late embryonic stages of blood-vessels and some associated connective tissue from the surrounding mesoderm. The impulse for the nervous differentiation of the dorsal ectoderm in primitive vertebrate ancestors probably arose from the fact that this part of the body is most directly exposed to stimulation from external sources. In accordance with the same physiological motive we find that the leading sense organs which serve as distance receptors (nose, ear, lens of eye) are likewise developed from this dorsal ectoderm, and the nervous parts of the eye are developed from the neural tube itself.

Early Embryology.—The central nervous system of the human body is first differentiated as an ectodermal neural plate in the dorso-medial region (Fig. 874). The lateral edges of this plate are pinched together dorsally to form a neural tube (Fig. 875), which then separates from the adjacent ectoderm, and the ganglia of the cerebrospinal nerves are developed chiefly from a ridge of cells known as the neural crest which lies on each side along the line of separation between the neural tube and the general ectoderm (Fig. 876). The cells which serve the functions of general sensibility in the root ganglia of the spinal and cerebral nerves arise from the neural crest. In lower vertebrates some cells of the neural crest are incorporated into the neural tube and here develop precociously for cutaneous innervation before

the spinal ganglia have reached functional maturity; these are the transitory giant cells found in the spinal cord of some fishes. They usually disappear before adult life is reached. It is probable that the mesencephalic nucleus of the trigeminus in mammals represents a persistent variant form of this mode of development, for the preponderance of evidence at the present time favors the belief that this nucleus

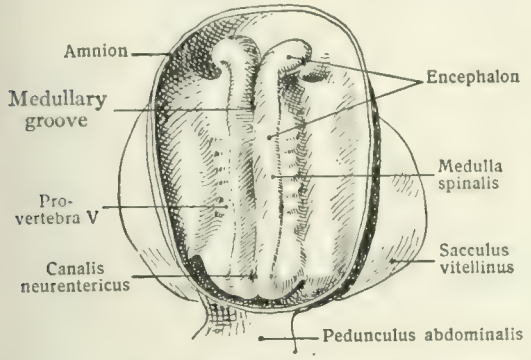

Fig. 874.—Neural Plate in an Embryo of Five to Six Primitive Segments. (After Keibel and Elze, from Keibel and Mall's Handbuch der Entwicklungsgeschichte des Menschen.)

gives rise to sensory fibers for deep sensibility in the muscles of the head.

In fishes some of the ganglia of the cerebral nerves receive cells both from the neural crest and from ectodermal placodes which are arranged in two series along the side of the head, a suprabranchial and an epibranchial series. These give rise respectively to ganglion cells of the acoustic and lateral line series of

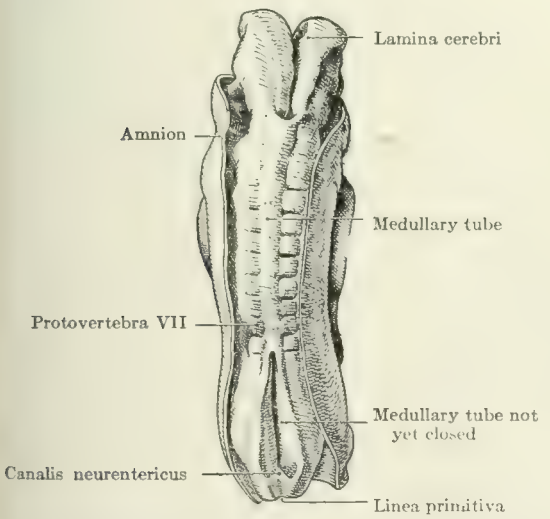

Fig. 875.—Eternod's Embryo of Eight Primitive Segments, 2.11 mm. long. (After Kollmann, from Keibel and Mall's Handbuch der Entwicklungsgeschichte des Menschen.)

nerves and of the gustatory nerves (Landacre). These series of placodes are known to occur in human embryos also and probably they contribute cells to the cerebral ganglia in similar fashion. Cf. the article *Cranial Nerves*.

Histogenesis.—The histogenesis of the neural tube starts from a simple columnar epithelium in the neural plate, which after the closure of the tube becomes a complex syncytium, the myelospongium, which rapidly increases in thickness in the lateral walls but retains its simple epithelial non-nervous character in the roof and floor of the tube. The original epithelial cells partially or completely lose their

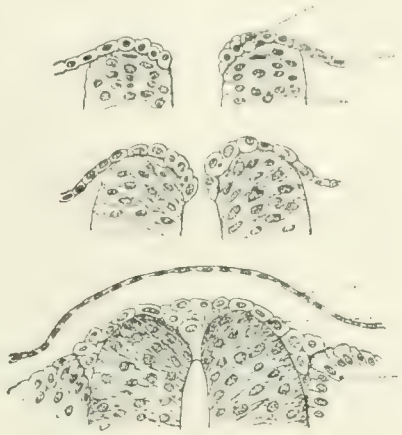

Fig. 876.—Three Stages in the Closure of the Neural Tube and Formation of the Neural Crest. From transverse sections of a human embryo of 2.5 mm. (13 pairs of primitive segments). (After von Lenhossék.)

identity, their nuclei proliferate rapidly near the ventricular surface and in later stages migrate outward embedded in strands of denser protoplasm which in general are radially disposed with many

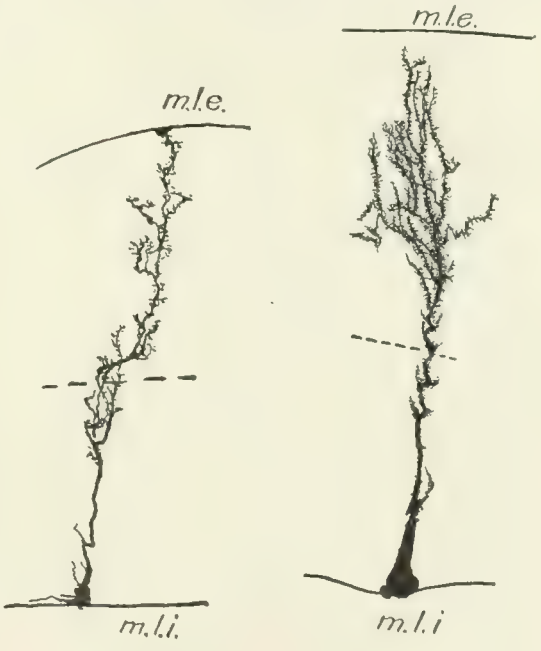

Fig. 877.—Two Ependyma Cells from the Brain of an Amphibian, Amblystoma tigrinum. × 150. *A*, From the wall of the thalamus of a larva; *B*, from the roof of the midbrain of an adult. *m.l.e.*, membrana limitans externa; *m.l.i.*, membrana limitans interna; the broken line between the external and internal limiting membranes marks the boundary between the stratum griseum (central gray layer) and the stratum album.

anastomoses. The nucleated radial filaments thus formed are termed spongioblasts and appear to be in part at least the collapsed remains of the original epithelial cells which retain their connection with

both the internal and the external limiting membranes. Their outer ends become vacuolated and finally much branched and usually lose their connection with the external limiting membrane. These constitute the ependyma cells whose expanded ventricular ends form the lining membrane of the ventricles and in later stages become ciliated.

In lower vertebrates where the walls of the brain tube are relatively thin the ependyma cells may retain permanently the relations just described for the spongioblasts and thus constitute the only supporting elements of the brain (Fig. 877). In the human brain many of the original spongioblasts become detached at both ends and thus become free glia cells.

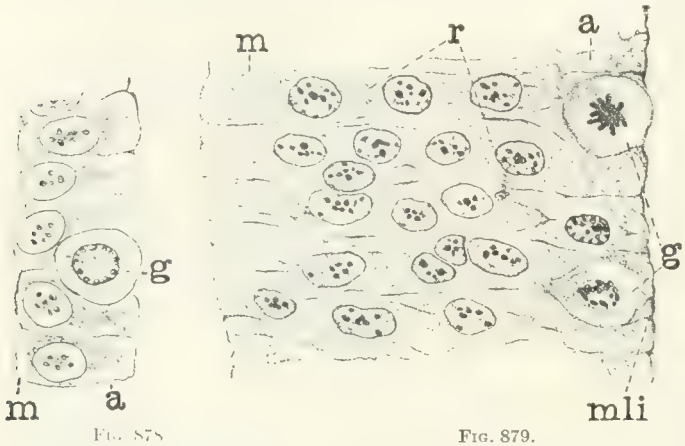

Fig. 878. Fig. 879.

Fig. 878.—From the Neural Plate of an Embryo Rabbit Shortly before the Closure of the Neural Tube. *a*, Inner zone; *g*, germinal cell; *m*, peripheral zone, position of outer marginal layer. (After His, from Bailey and Miller's Embryology.)

Fig. 879.—From the Neural Tube, Just after its Closure, of an Embryo Pig of 5 mm. *a*, Inner zone; *g*, germinal cell; *m*, peripheral zone, position of outer marginal layer; *mli*, internal limiting membrane; *r*, radial columns of protoplasm and remains of primitive epithelial cells. (After Hardesty from Bailey and Miller's Embryology.)

Around the periphery of the neural tube is a reticular area composed of a network of protoplasmic strands, the marginal layer, which for a considerable time remains free from nuclei. Within the inner nuclear layer of the original myelospongium larger free nuclei, the so-called germinal cells, appear and there multiply by mitosis. These cells gradually migrate outward, some becoming glia cells and others neuroblasts and ultimately neurones (Figs. 878 to 881). Later the neuroblasts tend to occupy the outer zone of the nuclear layer, thus forming the mantle layer, while the inner nuclear layer is occupied chiefly by ependymal nuclei and undifferentiated cells.

In general throughout the central nervous system the less highly differentiated neurones tend to retain in the adult their primitive position near the ventricle, thus constituting the "central grey," while the more highly specialized nerve centers are further removed from the source from which their neurones were proliferated. The cerebral and cerebellar cortex furnish the extreme illustrations of this principle.

Developmental Factors.—After the elements of the neural tube have been laid down in the manner already described, the subsequent development takes place under the influence of several distinct factors which do not always act in the same direction. The first of these factors is the primary segmental pattern of the early vertebrate ancestors. There are, in the second place, various mechanical factors which influence the form of the developing brain and its relations to surrounding non-nervous structures. And, third, the general function of the brain as the center of correlation between peripheral receptors and effectors involves various localized differentiations in response to the functional needs of the body. These local differentiations will vary in different parts of the brain in correlation with the systems of peripheral organs with which these several parts are in functional connection, and they will vary in different animals in response to the demands of their different modes of life.

Of these factors, the transverse segmentation is perhaps the most obvious in the early stages, both embryological (Fig. 882) and phylogenetic. Morphologists have, therefore, devoted a great deal of attention to metameric schemata of the brain and cerebral nerves. The primary segmental pattern is preserved in clearly recognizable form in the spinal nerve roots and ganglia and in the peripheral distribution of the cutaneous sensory nerves of the trunk. Both the sensory and the motor components of the muscular branches of the spinal nerves have deviated further from the original metameric arrangement, and within the spinal cord the demands of longitudinal correlation have greatly disturbed this arrangement. In fishes the region of the gills exhibits a segmentation of a very different type. The gills are visceral structures, and hence it follows that in the region of the branchial clefts the visceral components of the nerves are clearly segmented, while the somatic components are reduced, a condition which persists in the adult human brain, as shown by the composition of the VII., IX., X., and XI. pairs of cerebral nerves. The primary segmentation in front of the isthmus rhombencephali in all vertebrate brains has been so greatly obscured by secondary changes as to leave only uncertain traces in the adult.

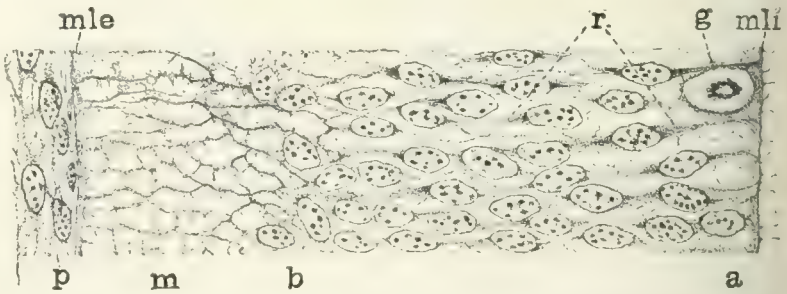

Fig. 880.—From the Neural Tube of an Embryo Pig of 10 mm. *a*, Inner zone; *b*, boundary between nucleated layer and marginal layer; *g*, germinal cell; *m*, peripheral zone; *mle*, external limiting membrane; *mli*, internal limiting membrane; *p*, rudiment of pia mater; *r*, radial column of protoplasm. (After Hardesty.)

Of the mechanical factors which have operated in the morphogenesis of the brain, we can mention only a few. In early stages the brain grows more rapidly in length than does the containing cranial cavity, thus producing a series of cerebral flexures (cf. Figs. 886, 891, 892, 894) which profoundly modify the course of subsequent development, though they in large measure disappear in the adult. The nutrition of

the brain as influenced by the vascular supply is also an important factor in morphogenesis, and in the adult the disposition of blood-vessels has an important bearing upon certain pathological processes. Thus, the middle cerebral artery is said to be especially liable to suffer from cerebral hemorrhage and anomalies in the circle of Willis and its associated vessels are more frequent in the insane than in normal brains. Under the stimulus of the researches of the late Professor Rudolf Burckhardt and some other neurologists much attention has been devoted recently to variations in the structure of the ependyma and other non-nervous tissues in different parts of the brain. Embryologically neuroblasts are formed only in the lateral walls of the neural tube, never in the roof plate or floor plate. Any nervous tissue which appears in the mid-dorsal and mid-ventral plane of the adult brain has entered from the lateral walls. The medial zone is, therefore, from both the embryological and phylogenetic standpoints the most conservative part of the brain. Much use has been made of this principle in determining the homologous parts of the brain in lower vertebrates and in recognizing the limits of the major subdivisions of the human brain.

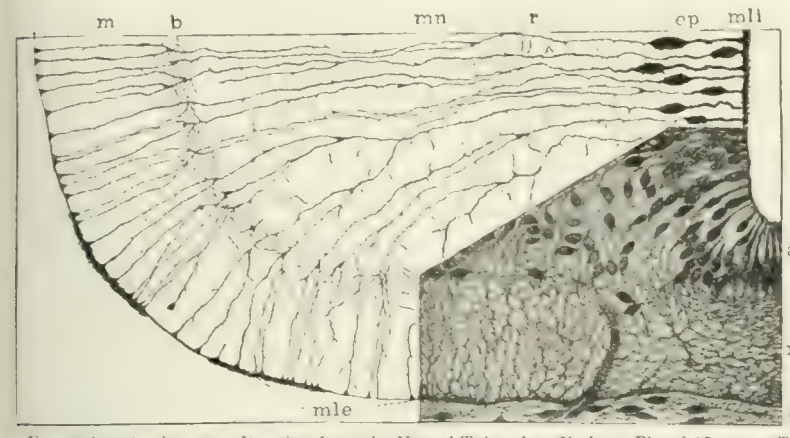

Fig. 881.—Combination Drawing from the Neural Tube of an Embryo Pig of 15 mm. The upper part of the figure was drawn from a preparation by the Golgi method. *cs*, Connective tissue syncytium in region of future pia mater; *ep*, ependymal layer; *mn*, mantle layer, or middle nucleated layer of neuroblasts resulting from the migration of nuclei from ependymal layer; *mv*, mantle layer in the mid-ventral line (floor plate). (After Hardesty from Bailey and Miller.)

But, after all, the principal factors in determining the form of the brain are the nerves themselves; and the cerebral architecture of every animal species has unquestionably been shaped chiefly under the influence of the peripheral sensori-motor mechanisms which characterize that animal's mode of life. A simple, mechanically determined type of action system can be carried on by means of a nervous system but little modified from the primary metameric type, as seen in the lowest vertebrates and many of the invertebrates. But the integration and coordination of function necessary in the more complex life of the higher vertebrates involves the development of correlation centers which control the activity. of many segments under the influence of remote and diverse types of sensory stimulation. By far the larger part of the brain is composed of such correlation centers. The increase in bulk of the massive walls of the brain as we pass forward from the spinal cord is correlated with the progressive change in the character of these correlation centers, as will appear beyond.

The histological unit of the nervous system was described above as the neurone. Neurones, however, never function independently, but only when connected in chains whose relations are physiologically determined. Accordingly, the real anatomical and physiological unit of the nervous system is not the neurone but the reflex arc, a chain of neurones consisting of a receptor, a coordinating center and an effector, with nerve fibers putting all in physiological connection, so arranged as to evoke an adaptive response by the effector upon stimulation of the receptor.

The analysis of the bodily organs into somatic and visceral systems is very fundamental. The somatic reflex systems enable the animal body to react adaptively to external stimuli. Their sense organs are exteroceptors (Sherrington) and the organs of response are the skeletal or somatic muscles. This somatic motor mechanism is itself very complex and it has its own system of intrinsic sense organs and sensory nerves (for muscle sense, joint and tendon sense, etc.) which have been termed by Sherrington the proprioceptors. The semicircular canals of the ear constitute the highest member of the proprioceptive system, which controls the automatisms of motor coordination, equilibration, etc., and which is a subsidiary part of the great somatic or

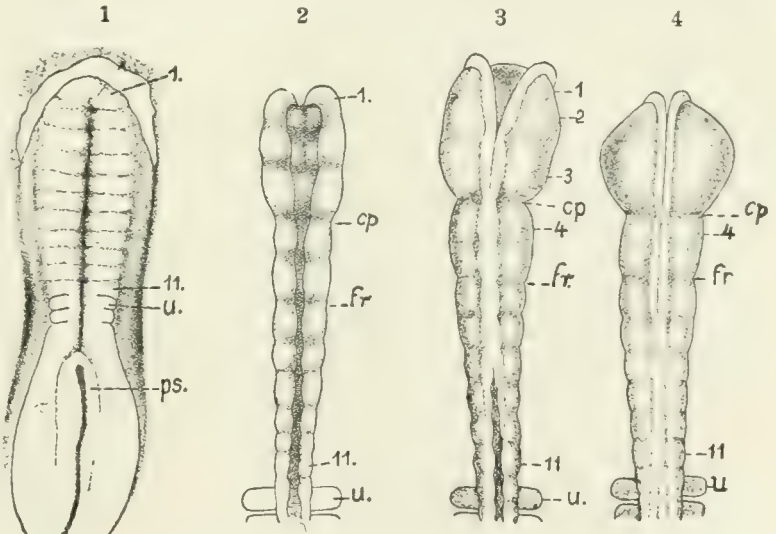

Fig. 882.—Chick Embryos Illustrating the Segmentation of the Neural Tube in Four Successive Stages of Incubation; One of Twenty-two Hours; Two of Twenty-four Hours; Three of Twenty-Five and One-half Hours; Four of Twenty-six Hours; Showing Respectively Two, Five, Six and Seven Primitive Mesodermal Segments. *cp*, Caudal limit of forebrain; *fr*, caudal limit of midbrain; *ps*, primitive streak, *u*, first mesodermal segment; 1–11, neuromeres. (After Hill from Bailey and Miller.)

exteroceptive mechanism. The visceral or splanchnic reflex systems are adapted for visceral responses to stimuli arising within the body. The visceral receptive organs are termed by Sherrington interoceptors.

While many lines of nervous conduction cross from one system to the other, exteroceptive stimuli sometimes producing visceral responses and conversely, nevertheless the most important reflex connections

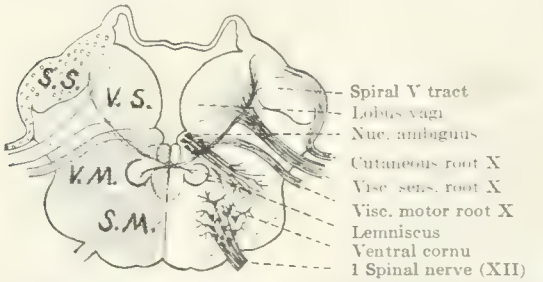

Fig. 883.—Diagrammatic Cross Section of the Medulla Oblongata at the Level of the Vagus Nerve of the Fish (*Prionotus carolinus*, the Sea Robin), to Illustrate the Arrangement of the Longitudinal Columns. *S.M.*, somatic motor column; *S.S.*, somatic sensory column; *V.M.*, visceral motor column; *V.S.*, visceral sensory column.

and correlation centers may be classified in these two groups. These two great divisions have been further analyzed into functional systems, each one of which performs a definite type of response to some particular kind of peripheral stimulation. The peripheral nerves, accordingly, have been analyzed into components in terms of their functional type. On the somatic side we have, among others, the various types of cutaneous nerves (tactile, thermal, etc.), the peripheral nerves serving the muscle sense, joint sense, etc., and the more highly specialized nerves of hearing and vision, together with their return efferent nerves to the respective somatic muscles concerned with these reflex systems. The visceral systems are less highly differentiated and integrated. They include afferent nerves from the digestive tract and its appendages and from other viscera and mucous surfaces, with the corresponding return efferent

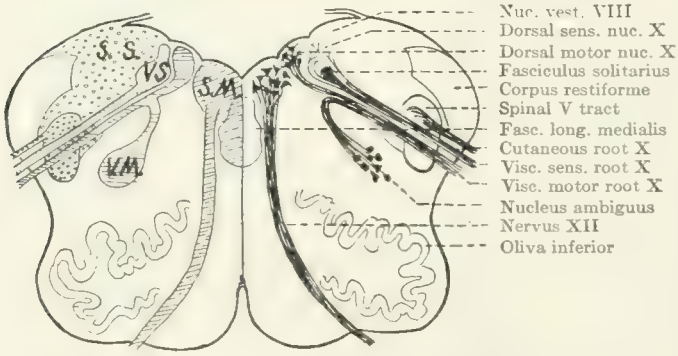

Fig. 884.—Diagrammatic Cross Section of the Human Medulla Oblongata at the Level of the Vagus Nerve; cf. Fig. 383. *S.M.*, Somatic motor column; *S.S.*, somatic sensory column; *V.M.*, visceral motor column; *V.S.*, visceral sensory column.

paths, distributed through the sympathetic nervous system; and also some more highly specialized systems represented in the cerebral nerves, notably the nerves of taste and the motor nerves supplying striated muscles of visceral type derived phylogenetically from the gill muscles of fishes. These special visceral motor nerves arise from the ventrolateral series of motor nuclei of the medulla oblongata in the V., VII., IX., X., and XI. cerebral nerves. The olfactory system is probably a still more highly specialized derivative of the visceral sensory system.

In the trunk region the peripheral nerve components tend to be arranged in a segmental way, each spinal nerve repeating approximately the same plan. Within the spinal cord, however, the components are completely rearranged in longitudinal

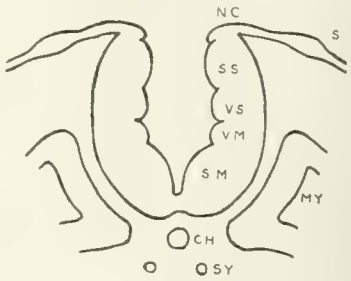

Fig. 885.—Diagrammatic Cross Section of the Embryonic Neural Tube During the process of Invagination, to Illustrate the Relations of the Longitudinal Columns to the Skin and other Adjacent Structures. *CH*, notochord; *NC*, neural crest; *MY*, myotome; *S*, sensilla; *SM*, somatic motor column; *SS*, somatic sensory column; *SY*, sympathetic ganglia; *VM*, visceral motor column; *VS*, visceral sensory column.

columns which cut across and obscure the primary metamerism. In the head region each of the more highly specialized sensory components tends to be concentrated into a few nerves or only one, an adaptation which presents obvious advantages for the simplification and unification of secondary reflex paths.

Functional Analysis.—In accordance with the functional analysis which we have just outlined, the brain is found to be divided into longitudinal columns with which the primary functional systems are related and within which their correlation tissues are elaborated. This applies especially to the brain stem below the thalamus. The higher correlation centers of the prosencephalon (suprasegmental centers of Adolf Meyer) show less clearly their relationship with the fundamental longitudinal columns, but they can be classified in accordance with the same physiological principles, as will appear beyond.

In the medulla oblongata of fishes, where the amount of correlation tissue is less than in man and where the arrangement of the intrinsic centers is less obscured by long conduction paths from distant parts of the nervous system, the functionally defined longitudinal columns appear anatomically as well-defined ridges in the walls of the fourth ventricle (Fig. 883), whose arrangement is seen to be similar to that of the spinal cord; viz., the somatic sensory and motor columns occupying respectively the dorsal and ventral parts of the lateral wall, the visceral sensory and motor lying between. In the human oblongata (Fig. 884) the arrangement is essentially similar, though with numerous changes in the details. This arrangement probably grows out of the topographic relations of the neural epithelium to surrounding structures. Thus, the lateral parts of the neural plate (cf. Fig. 874) were originally in intimate contact with the great somatic receptive surface of the skin, while after the invagination of the neural tube its ventrolateral wall, derived from the medial part of the neural plate, lies in immediate contact with the myotome, from which the somatic muscles are to be derived (Fig. 885). The visceral centers,

which are relatively feebly developed in the trunk region of all animals and in the oblongata of the lowest vertebrates, lie between.

The primary sensory and motor centers of the brain, accordingly, are found to lie in four longitudinal columns on each side, arranged from dorsal to ventral in this order: somatic sensory, visceral sensory, visceral motor, somatic motor. The subsidiary functions within each of these great systems tend to be segregated from the others and concentrated in a definite region. For instance, in the somatic sensory column of the medulla oblongata the cerebral general cutaneous nerves nearly all enter the brain by the nervus trigeminus, with much smaller components in the IX. and X. nerves; and all of these fibers enter the spinal V. tract and its associated grey matter. But the specialized derivatives of the somatic sensory system represented in the vestibular and cochlear nerves discharge into distinct areas within the somatic sensory column, the vestibular and cochlear nuclei, while muscular sensibility is probably chiefly served by the mesencephalic nucleus of the trigeminus. Each of these functionally differentiated areas has developed its own system of secondary associational tracts. The associational tissue was developed first in the reticular formation interpolated between the primary sensory and motor areas, a tissue so arranged as to facilitate the discharge from the several receptive centers into their respective motor centers in such a way as to effect the adaptively useful response rather than mere random activity (Fig. 912, 17). This tissue is present throughout the entire

Posterior cerebral vesicle.	I. Medulla oblongata	Myelencephalon I. (Afterbrain).		Rhombencephalon I.–III. (*Rautenhirn*).		Encephalon I. VI. (Brain).
	II_1. Pons.	Metencephalon II. (Hindbrain).				
	II_2. Cerebellum					
	III.	Isthmus rhombencephali III.				
Middle cerebral vesicle.	IV_1. Pedunculi cerebri	Mesencephalon IV. (Midbrain).				
	IV_2. Corpora quadrigemina					
Anterior cerebral vesicle.	V_1. Pars mammillaris hypothalami (Hypothalamus vice pars mam. and pars optica).		Diencephalon V. (Interbrain).	Prosencephalon V. and VI. (Forebrain).	Cerebrum IV. VI. (*Grosshirn*).	
	V_2. Thalamus	Thalamencephalon V_2–V_4.				
	V_3. Metathalamus					
	V_4. Epithalamus					
	VI_1. Pars optica hypothalami		Telencephalon VI. (Endbrain).			
	VI_2. Corpus striatum	Hemisphærium VI_2 VI_4.				
	VI_3. Rhinencephalon					
	VI_4. Pallium					

length of the cerebrospinal axis, but in some parts of the medulla oblongata it is more highly developed and condensed into special areas. The tegmentum of the midbrain is the direct forward extension of these areas.

The reticular formation is the parent associational tissue from which all higher correlation centers have been differentiated. Anatomists distinguish a formatio reticularis alba, in which medullated nerve fibers predominate, from a formatio reticularis grisea, in which nerve cells and unmedullated fibers predominate. Both forms consist fundamentally of neurones whose dendrites extend into the primary sensory centers and whose axones discharge into one or more motor centers of the same or the opposite side of the brain. Thus many different sense organs may be brought into relation with a single motor organ through a common final path, or a given sense organ may be brought into relation with several different motor organs. This is the mechanism by which reflexes are compounded and integrated.

As we pass forward into the higher regions of the brain, more complex and sharply circumscribed correlation centers are differentiated, so arranged that a sensory stimulus must pass successively through several such centers, in each of which it may come into physiological relation with other types of simple sensory impulses and various combinations of such sensory impressions before it is finally discharged into a motor center. These higher association centers, like the elementary reticular formation from which they were derived, of course serve as intermediaries between the receptors and the effectors, but they are in many cases under the dominating influence of individual receptors or of special systems of muscles. In this case the association center may be spoken of as an optic or acoustic correlation center or as a motor correlation center.

The physiological factors which have just been considered play a dominant rôle in the development of the form of the brain. In the first place, the proliferation of neuroblasts takes place most rapidly in the dorsolateral and ventrolateral parts of the early neural tube, resulting in a thickening of the wall in these regions and the formation by arrest of development of a longitudinal ependymal sulcus between them. This sulcus limitans is the most fundamental landmark of the brain, for it separates on each side a ventrolateral motor plate (the basal or hypencephalic plate of His) from a dorsolateral sensory plate (the alar or epencephalic plate of His). The position of the sulcus limitans is shown in Fig. 887. This limiting sulcus in some lower brains is preserved in the adult, but in the human brain it disappears except for a short distance in the floor of the fourth ventricle. As already stated, nervous elements never originate within the roof plate and floor plate of the neural tube, though they may migrate across these plates or into them in later embryonic stages. The chorioid plexuses of the third and fourth ventricles are formed by local expansions of the non-nervous roof plate, to which the pia mater and its blood-vessels become attached.

Subdivision of the Brain.—For our knowledge of the sequence of form changes in the developing human brain we are chiefly indebted to the researches of His and the series of wax models which he has published. Upon these researches was also based the scheme of subdivision of the brain and its terminology, officially adopted by the nomenclature commission of the German Anatomical Society at Basle in 1895, which is now widely used throughout the world (usually termed the BNA). The outline of this scheme is presented in the accompanying table and in Figs. 887, 891, 892, 893. Compare also His (1895) and Barker (1907).

There is a discrepancy between the subdivision of the prosencephalon as given in the BNA schedule and in the accompanying explanatory notes by Professor His, in that in the latter the pars optica hypothalami is joined to the telencephalon, as given in the table as here reprinted from the notes of His, while in the BNA schedule this part is classified with the diencephalon. Subsequent research makes it evident that the original usage of His (perhaps with slight modification) rather than that of the BNA should here be followed; cf. Johnston (1909).

Various other modifications of the BNA scheme have been suggested, especially in view of the data of comparative neurology, of which the following seem to the present writer of sufficient importance to require recognition. The rhombencephalon is a natural division, but of its subdivisions, the isthmus

rhombencephali as a transverse segment of the brain tube seems unnecessary. The isthmus should rather be regarded merely as a plane of separation between the mesencephalon and the rhombencephalon. The metencephalon and myelencephalon, as defined by His, are not natural subdivisions. It accords better with both embryology and phylogeny to separate the rhombencephalon into a primitive segmental part,

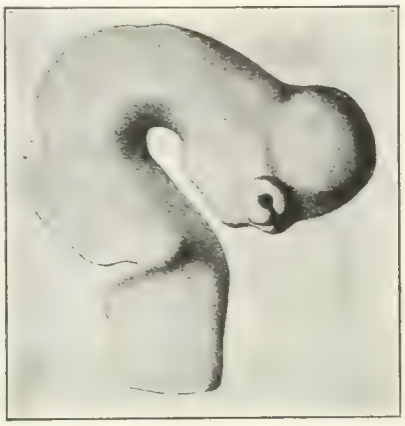

FIG. 886.—Side View of a Model of the Brain of a Human Embryo at the End of the First Month. (After His, from Bailey and Miller's Embryology.)

the medulla oblongata, and a secondary suprasegmental part, the metencephalon, comprising the cerebellum and pons, these latter, together with the brachium pontis, encircling the more primitive medulla oblongata without involving any important changes within it. The medulla oblongata may then be subdivided into (1) the myelencephalon, which in fishes innervates the gill region and in all vertebrates serves chiefly respiratory and other visceral functions, and (2) the facial part of the oblongata, comprising the cerebral region of the V. and VII. nerves for the sensory and motor innervation of the face. The centers for the VIII. nerve (and the lateral line nerves of fishes) lie in the facialis segment and from them the cerebellum has been differentiated. The writer would, therefore, subdivide the rhombencephalon as follows:

Rhombencephalon.
- Medulla oblongata.
  - Myelencephalon.
  - Pars facialis medullæ.
- Metencephalon.
  - Cerebellum.
  - Pons.

Development.—The form of the human brain at the end of the first month of intrauterine life is shown in Fig. 886, and the subdivisions of the brain at this age, as defined by His, are indicated in Fig. 887. The arrangement of the primary longitudinal columns in the medulla oblongata of an embryo of about the same age is seen in Fig. 888, where the sulcus limitans separates the dorsolateral sensory columns (alar plate) from the ventrolateral motor columns (basal plate). The visceral motor and somatic motor columns are shown by the positions of the motor nuclei respectively of the X. and XII. cerebral nerves. In the dorsolateral plate the visceral and somatic columns are not clearly differentiated at this age. The position of the visceral sensory column is indicated by the tractus solitarius, which receives the visceral sensory roots of the VII., IX., and X. cerebral nerves; cf. Fig. 884. The positions of the cerebral nerve roots in this embryo are indicated in Fig. 888, where it is evident that the motor nerve roots are arranged in two series, a ventral somatic motor (XII., VI., IV., III) and a lateral visceral motor (XI., X., IX., VII., V.). The sensory roots are arranged in a still different series more dorsally placed, in which, however, it is not possible in this figure to distinguish a visceral sensory from a somatic sensory line. A study of the composition of the sensory roots in the adult shows that the V. root contains only (or chiefly?) somatic sensory fibers, the VII. root only visceral sensory, the VIII. specialized somatic sensory, the IX. and X. chiefly visceral sensory, with a small somatic sensory component, the visceral and somatic sensory columns within the medulla oblongata being here clearly separate (cf. Fig. 905).

In embryos of about this age the upper border of the dorsolateral plate in the medulla oblongata becomes strongly folded by a rapid proliferation of neuroblasts to form the rhombic lip (Figs. 889 and 890). From this lip neuroblasts migrate ventrally at a later period to form the olivary bodies and other important correlation centers in the reticular formation. The nuclei of the pons are subsequently formed from the same region of the rhombic lip along the caudal border of the lateral recess of the fourth ventricle by a migration of neuroblasts close to the surface of the oblongata forward and downward to the pons flexure (Essick). At a still later period the rhombic lip also gives rise to the cerebellum, whose cellular elements migrate dorsally into the roof plate and there proliferate.

Figs. 891 and 892 illustrate the form changes in the various regions of the brain between the sixth week and the third month of development, and the adult relations are seen in Fig. 893. The flexures of the brain attain their maximum development in an embryo of about seven and one-half weeks (Fig. 894).

The mesencephalon departs less from the primitive relations of the neural tube than do most other parts of the brain. In the ventrolateral lamina the somatic

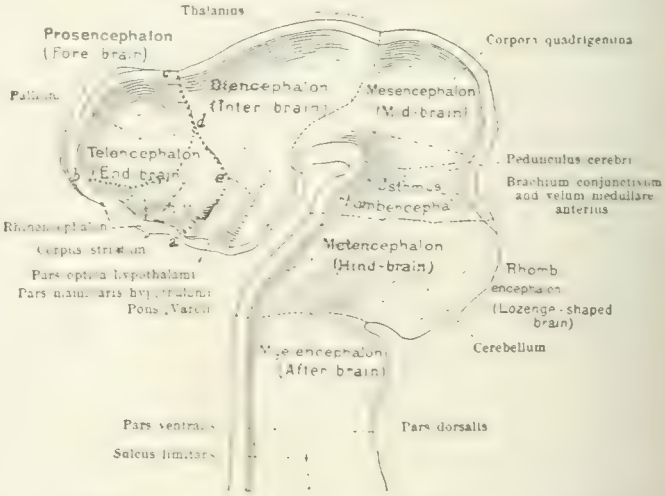

FIG. 887.—Vertical Medial Section of the Model Shown in Fig. 886, Indicating the Position of the Sulcus Limitans and of the BNA Subdivisions of the Brain. (After His, from Spalteholz' Atlas.)

motor system is represented in the nuclei of the III. and IV. cerebral nerves, the former nucleus including also a visceral motor component for the ciliary muscles of the eyeball by way of the ciliary ganglion. The remainder of the ventral lamina is occupied by fibers of passage between higher and lower centers, like the pyramidal tracts, and by the association tissues of the tegmentum in which somatic motor

functions predominate. The most important efferent tracts from the cerebellum make their connections here in the nucleus ruber (Fig. 895).

In the dorsolateral lamina of the midbrain the mesencephalic nucleus of the V. nerve probably represents the primitive somatic sensory column (Johnston), and the remainder of the tissue which constitutes the tectum mesencephali is devoted chiefly to the coordination of somatic sensory impressions. In lower vertebrates fibers of general cutaneous sensibility enter all parts of the tectum by way of the lemniscus, and the same probably holds true in man. But in the latter case there are in addition two highly differentiated somatic sensory systems, (1) the lateral lemniscus, bearing acoustic impressions from the cochlea, and (2) the optic tracts, bearing visual impressions from the retina. These tracts determine respectively the development of the inferior and superior colliculus of the corpora quadrigemina.

The development of the prosencephalon is much more complex, for here the primary segmental apparatus has been overshadowed by suprasegmental correlation centers of the most intricate character. There are no peripheral motor nerves in this region; accordingly, the ventrolateral lamina is greatly reduced and the sulcus limitans drops rapidly ventrally into the preoptic recess (Figs. 896, 887).

The vertical medial section through the brain gives valuable morphological landmarks, since the organs in this plane have suffered least modification through unctional adaptation because of the fact that no neuroblasts are differentiated within the roof plate and floor plate of the neural tube. In fact, a series of such sagittal sections through embryonic and adult brains of different animals shows a surprising uniformity from the lowest to the highest vertebrates; cf. Burckhardt (1895). Such a section from a three-day embryo of the sturgeon is shown in Fig. 897. A comparison of this with medial sections of the embryonic human brain (cf. Figs. 887, 891, 892) shows a much closer resemblance than would be seen by a comparison of the external forms of these brains. In Fig. 897 the velum transversum (*vt*) marks the boundary dorsally between the diencephalon and the telencephalon. The corresponding position in the human brain is probably indicated by the dotted line *c–d* in Fig. 887. The chorioid plexus of the third ventricle develops from the caudal limb of the velum transversum and the lateral plexuses of the hemispheres from its anterior limb. (The mode of origin of the lateral plexuses is, however, controverted.)

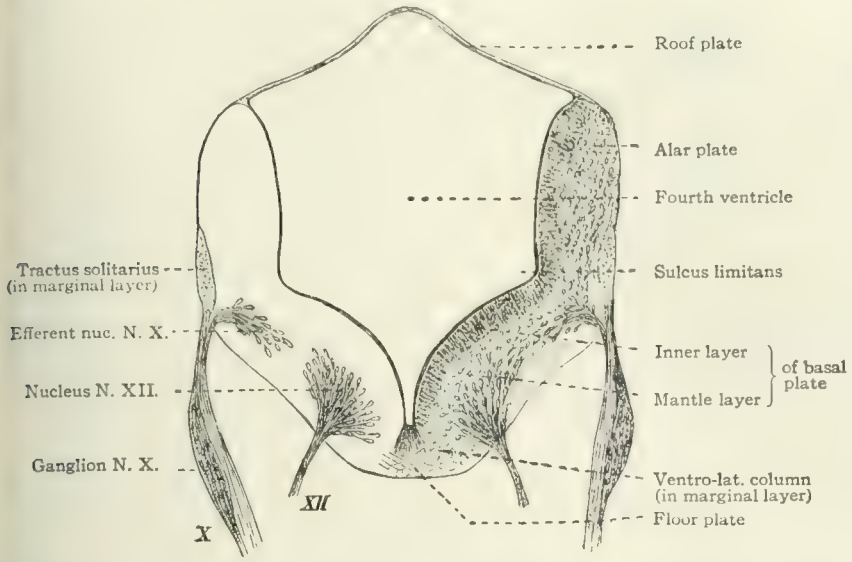

Fig. 888.—Transverse Section Through the Medulla Oblongata of a Human Embryo of 10.2 mm. (Fifth Week), Illustrating the Arrangement of the Longitudinal Columns; cf. Figs. 883, 884. (After His, from Bailey and Miller's Embryology.)

The tissue lying ventrally of the sulcus limitans in the diencephalon contains motor correlation centers. The more caudal part of this, near the tegmentum of the midbrain, is of somatic motor type, discharging directly into the cerebral peduncle and tegmentum, while that farther forward in the pars mammillaris hypothalami serves chiefly olfactory and visceral functions. The remainder of the diencephalon and all of the telencephalon except a very small vestige in the vicinity of the optic chiasma (Johnston) develops from the dorsolateral, or sensory lamina of the neural tube.

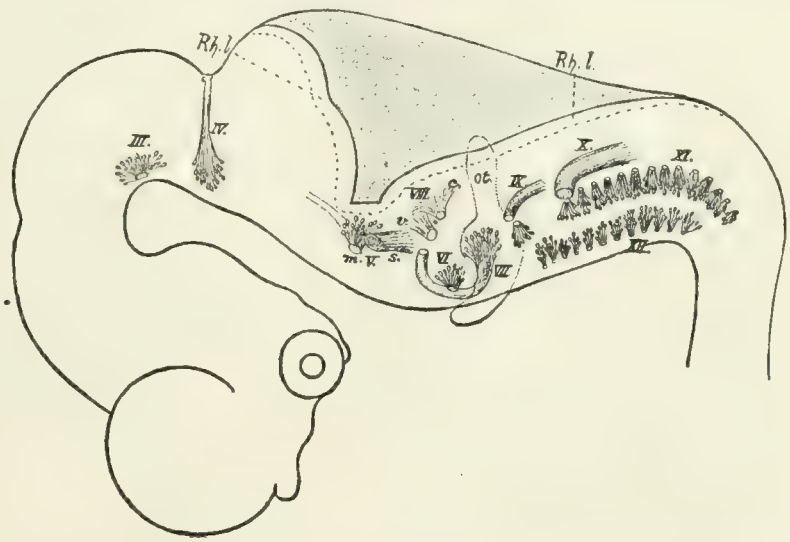

Fig. 889.—Lateral View of the Brain of the Same Embryo Shown in Fig. 888, showing the Roots of the Cerebral Nerves. *III*, oculomotor; *IV*, trochlear; *V*, trigeminus (*m*, efferent root, *s*, afferent root); *VI*, abducens; *VII*, facial; *VIII*, acoustic (*c*, cochlear root, *v*, vestibular root); *IX*, glossopharyngeus; *X*, vagus; *XI*, spinal accessory; *XII*, hypoglossus; *ot.*, auditory vesicle; *Rh. l.*, rhombic lip. (After His, from Bailey and Miller's Embryology.)

Two pairs of important lateral evaginations arise from this part of the neural tube. One pair arises from the sensory lamina of the diencephalon and produces the lateral eyes; the other pair arises farther forward in the telencephalon and produces the cerebral hemispheres. The optic evaginations begin at the lateral border of the neural plate before it has closed up to form the neural tube (Fig. 898) and rapidly enlarge to form the optic vesicles, attached by slender epithelial stalks which later become the optic nerves (Fig. 899). The attachment of the optic stalk secondarily shifts from the dorsal to the ventral side of the diencephalon (Fig. 886), where in the adult it marks the ventral boundary between the telencephalon and the diencephalon (Johnston, 1909). In sharks Locy (1895) finds the optic pits present in the open neural plate at a very early stage and caudad of them several pairs of similar but smaller pits which he terms accessory optic vesicles. The members of one of these pairs fuse in the middorsal line to form the epiphysis; the others disappear or are incorporated into other structures. The epiphysis, or pineal body, in some lower vertebrates extends through a foramen in the top of the skull and there develops a well-formed eye, with lens, retina, and a pineal nerve. In man this organ is vestigeal.

The diencephalon is early divided into three principal parts, the hypothalamus, the epithalamus and the thalamus. The hypothalamus lies wholly within the primary ventrolateral or motor lamina and receives directly the great descending olfactory tracts from the basal olfactory nuclei of the telencephalon and the columna fornicis, which is the great descending projection tract from the hippocampus, or olfactory cerebral cortex. In lower vertebrates it is known to receive gustatory tracts also. Its functions are obscure; it probably serves for the correlation of olfactory, gustatory and general visceral reflexes and their discharge into the motor centers of the tegmentum.

The epithalamus is developed wholly within the dorsolateral or sensory lamina. It includes the epiphysis or pineal body and some adjacent gray centers, of which the most important is the habenula. The latter, like the hypothalamus, receives important olfactory tracts from the basal olfactory nuclei and from the hippocampus of the telencephalon (these entering by way of the stria medullaris thalami) and discharges by way of the fasciculus retroflexus of Meynert into the tegmentum.

The thalamus is developed partly from the motor lamina, but chiefly from the sensory lamina above the sulcus limitans (Figs. 887, 896, 891, 892). In the embryo of five weeks (Fig. 896) the motor part is seen as a distinct eminence in front of the tegmental swelling and above the hypothalamus, while the sensory part is as yet undifferentiated. In later stages (Figs. 891 and 892) the sensory part increases rapidly in size and in the adult comprises by far the greater part of the thalamus. The thalamus, accordingly, may conveniently be divided into a pars dorsalis, devoted chiefly to the correlation of somatic sensory impulses, and a pars ventralis, devoted to correlations of efferent impulses and their direct discharge into the motor centers of the tegmentum and lower centers. This distinction is very fundamental, though commonly unrecognized.

The telencephalon includes the most anterior segment of the neural tube. The cerebral hemispheres begin as lateral outgrowths from this segment (Fig. 886), which finally involve the whole of the lateral walls except the region immediately adjacent to the optic chiasma and preoptic recess (preoptic nucleus, or ganglion basale opticum). In the hemisphere there is an olfactory division, the rhinencephalon, and a non-olfactory, or somatic division.

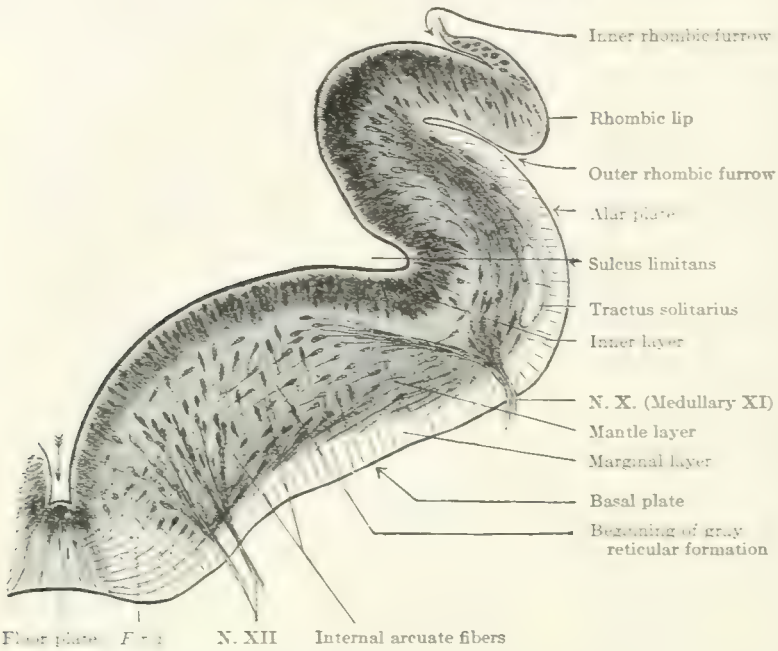

Fig. 890.—Half of a Transverse Section of the Medulla Oblongata of a Human Embryo of 9.1 mm. (During the Fifth Week). *F.r.a.*, beginning of the white reticular formation. (After His, from Bailey and Miller's Embryology.)

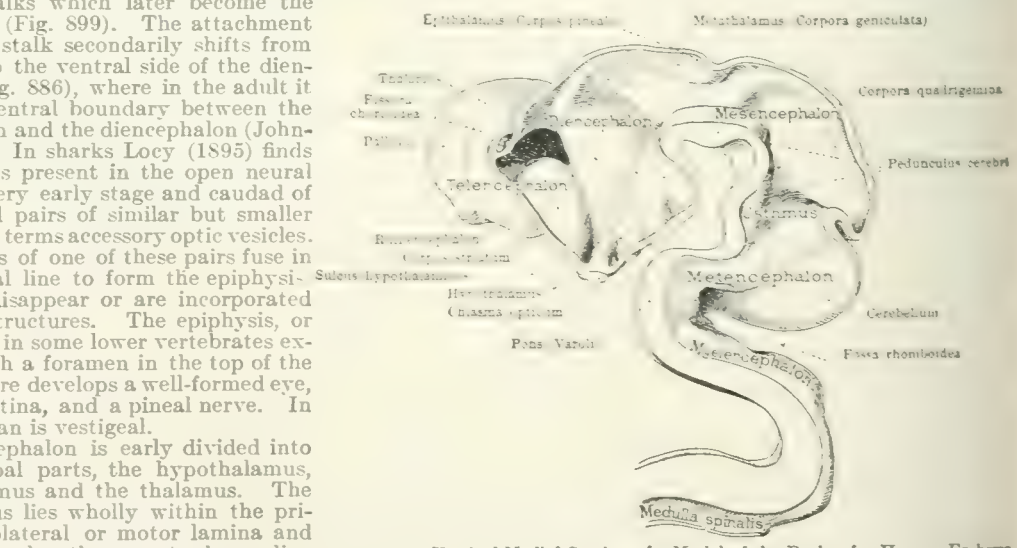

Fig. 891.—Vertical Medial Section of a Model of the Brain of a Human Embryo of 13.6 mm. (Sixth Week). (After His, from Spalteholz' Atlas.)

Further consideration of the development and general morphology of the thalamus and cerebral hemispheres will be taken up in connection with their adult anatomy in the next section.

Special Anatomy.—The brain is the great organ of correlation by means of which the various parts of the body are enabled to work together in harmony and the whole organism to make the appropriate responses to the environing forces of the outside world. Its external form has been determined chiefly by the space requirements of its correlation centers under the influence of phylogenetic and embryological factors, some of which have already been summarized. The entire brain is an elaboration of the anterior end of the embryonic neural tube, and it retains its embryological character of a hollow organ whose parts represent various unequal thickenings of the walls of the primitive tube. The ventricles of the brain are simply the persistent lumen of this tube. Their form in the adult brain is shown in Fig. 900.

The various parts of the brain stem are concerned with the simple primitive reflexes and with certain more complex correlations, chiefly on the reflex and instinctive plane, while the cerebral cortex is devoted largely to those higher types of correlation which are involved in the conscious life. In each part of the brain there is a primitive intrinsic reflex apparatus, consisting of certain peripheral nerves and their primary cerebral centers (these were orginally segmentally arranged), together with the related correlation neurones in the reticular formation; and in some parts of the brain there are also present suprasegmental correlation centers of a higher order. The intrinsic reflex mechanisms are functionally analyzed into four groups, somatic sensory, visceral sensory, visceral motor and somatic motor, which are arranged for purposes of fore-and-aft correlation in four longitudinal columns on each side of the brain and which are connected with each other by a complex system of crossed and uncrossed association tracts (see Figs. 883, 884, 888, 889).

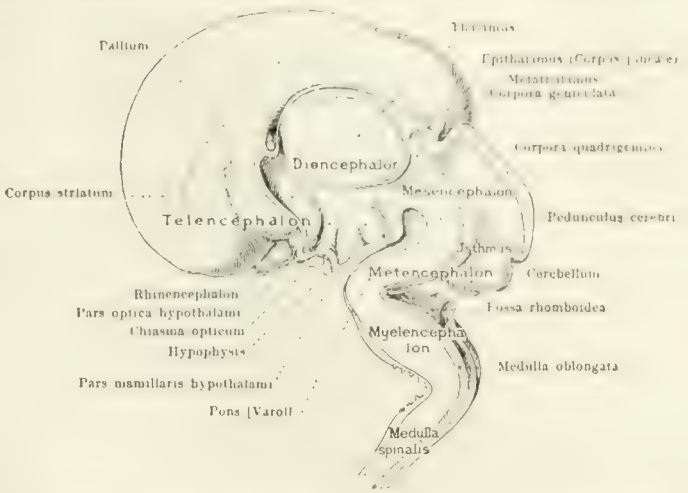

Fig. 892.—Vertical Medial Section of a Model of the Brain of a Human Fetus in the Third Month. (After His, from Spalteholz' Atlas.)

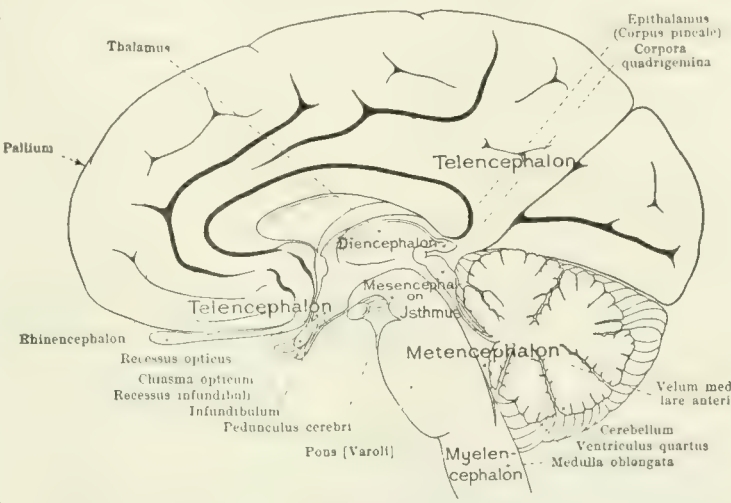

Fig. 893.—Vertical Medial Section of the Adult Human Brain. (From Spalteholz' Atlas.)

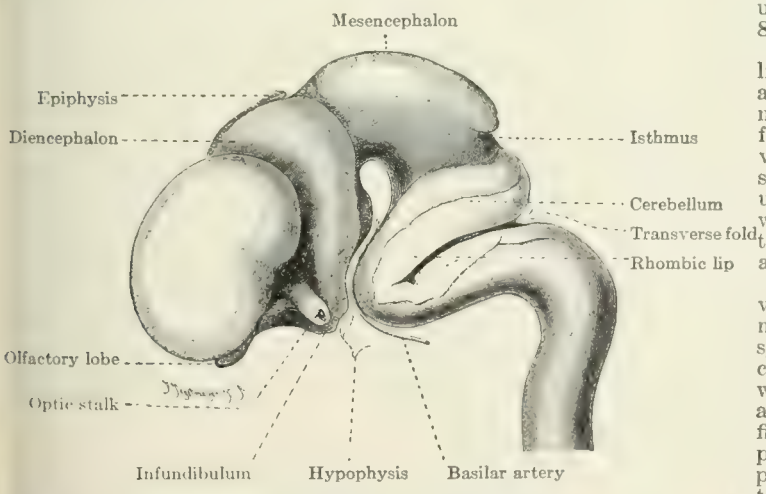

Fig. 894.—Lateral View of a Model of the Brain of a Human Embryo of 18.5 mm. (7½ Weeks). (After His, from Bailey and Miller's Embryology.)

In the following discussion we shall limit ourselves, for the most part, to a consideration of the correlation mechanisms and treat of external form only as incidental to this. A ventral view of the entire brain is seen in Fig. 901. We shall first take up the anatomy of the brain stem, whose superficial appearance from the ventral side is seen in Fig. 902 and from the dorsal side in Fig. 903.

The Brain Stem, General.—On the ventral surface of the brain stem the most important structure is the great system of descending fibers from the cerebral hemispheres. These fibers, which compose the pedunculi cerebri and pyramids, are crossed superficially by those of the pons, which put the descending fibers of the pedunculi cerebri into relation with the hemispheres of the cerebellum. At the lower end of the medulla

oblongata most of the fibers of the pyramidal tract disappear from the surface, decussate across the ventral fissure and turn dorsal to continue backward as the fasciculus cerebrospinalis lateralis of the spinal cord (Figs. 902, 909). The lateral surface of the medulla oblongata receives a strong tract of fibers

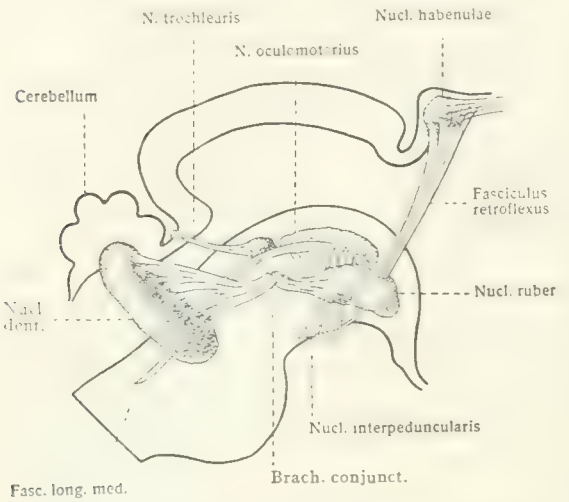

FIG. 895.—Reconstruction of the Midbrain of a Human Fetus of 80 mm. (Mall's Collection, No. 172), seen from the Right Side, Showing the Origin of the Brachium Conjunctivum from the Nucleus Dentatus of the Cerebellum, its Decussation and Termination in the Nucleus Ruber; Also the Mesencephalic Connections of the Nucleus Habenulæ and III and IV Nerves. (After Streeter, from Keibel and Mall's Handbuch der Entwicklungsgeschichte des Menschen.)

(Fig. 902, *cl.*) from the lateral funiculus of the spinal cord. Most of these terminate in the oblongata, but some of them pass farther forward, carrying impulses of the tactile, temperature and pain systems from the spinal cord forward into the lemniscus (Henry Head); cf. Fig. 989, *f. s.–t.* On the dorsal surface of the medulla oblongata are found the funiculus cuneatus and the

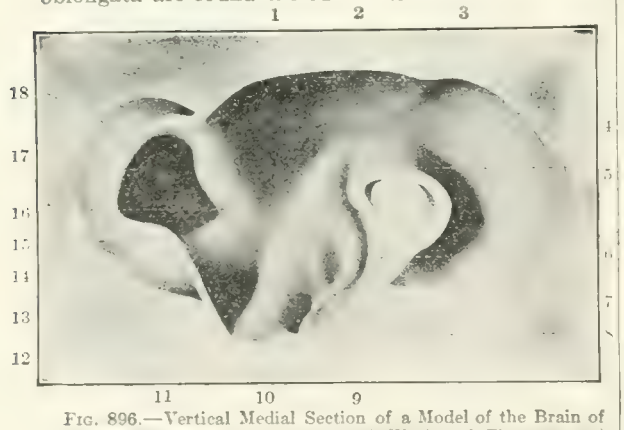

FIG. 896.—Vertical Medial Section of a Model of the Brain of a Human Embryo of 10.2 mm. Fifth Week; cf. Figs. 888 and 889. The sulcus limitans is visible in the figure (cf. Fig. 887). Its anterior end, marked sulcus hypothalamicus, terminates in the recessus preopticus. 1, Diencephalon; 2, thalamus; 3, pineal region; 4, mesencephalon; 5, tegmental swelling; 6, mammillary region; 7, hypothalmus; 8, tuber cinereum; 9, recessus infundibuli; 10, hypophyseal pouch; 11, recessus preopticus; 12, corpus striatum; 13, lamina terminalis; 14, post. olfact. lobe; 15, ant. olfact. lobe; 16, sulcus hypothalamicus; 17, foramen of Monro; 18, pallium. (After His, from Bailey and Miller's Embryology.)

clava, within which are the terminal nuclei respectively of the fasciculus cuneatus and gracilis of the spinal cord. These nuclei are important correlation centers for the ascending systems of spinal conduction for deep sensibility, muscular coordination, posture, etc. The two clavæ divaricate around the lower end of the fourth ventricle (calamus scriptorius), whose

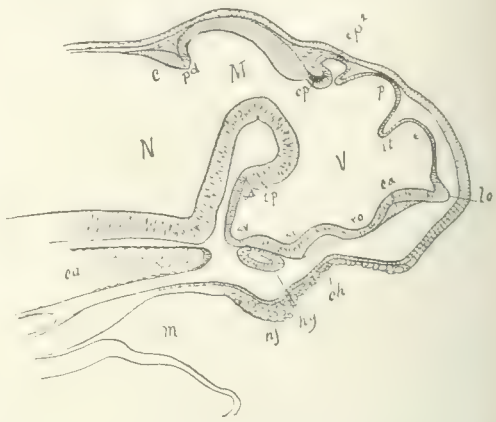

FIG. 897.—Medial Longitudinal Section through the Head of a Larva of the Sturgeon (Acipenser sturio) Three Days Old. *c*, Cerebellum; *ca*, commissura anterior; *cd*, chorda dorsalis; *ch*, optic chiasma; *cp*, commissura posterior; *e*, roof of the telencephalon (lamina supraneuroporica, Johnston); *ep*,[2] epiphysis or pineal body; *hf*, adhesive organ; *hy*, hypophysis; *lo*, lobus olfactorius impar (the neuroporic recess, marking the dorsal border of the neuropore, Johnston); *M*, midbrain; *m*, mouth; *N*, rhombencephalon; *p*, parencephalon or prepineal roof of the diencephalon; *pd*, plica dorsalis; *ro*, recessus preopticus; *sd*, saccus dorsalis; *si*, sinus postopticus; *sv*, saccus ventralis; *tp*, tuberculum posterius; *V*, prosencephalon; *vt*, velum transversum. (After von Kupffer.)

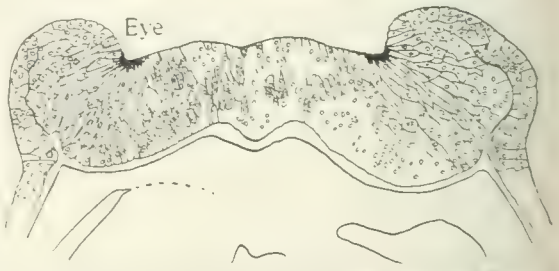

FIG. 898.—Cross Section through the Medullary Plate of Amblystoma punctatum, Showing the Positions of the Eye Spots. (After Johnston.)

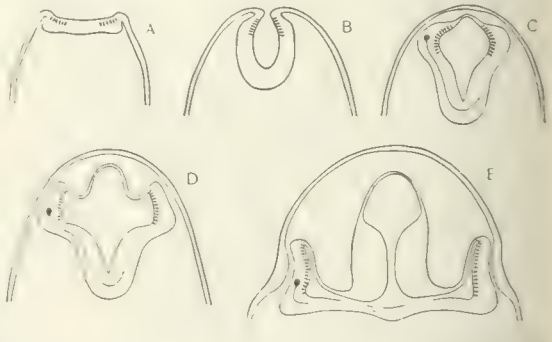

FIG. 899.—A Series of Diagrams to Illustrate the Origin and Mode of Formation of the Optic Vesicle in Vertebrates. (After Johnston.)

membranous roof is widely dilated to form the chorioid plexus of the fourth ventricle. The line of contact of this membrane with the massive wall is the tænia of the fourth ventricle. In the calamus scriptorius the tænia is thickened to form the obex.

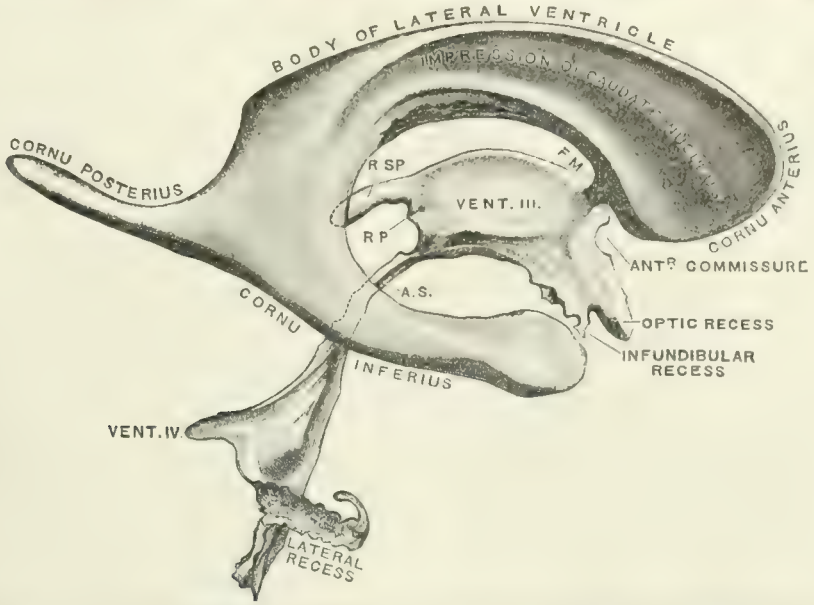

FIG. 900.—Profile View of a Cast of the Ventricles of the Brain. *A.S.*, Aqueduct of Sylvius; *F.M.*, foramen of Monro; *R.P.*, recessus pinealis; *R.SP.*, recessus suprapinealis. (After Retzius, from Cunningham's Anatomy.)

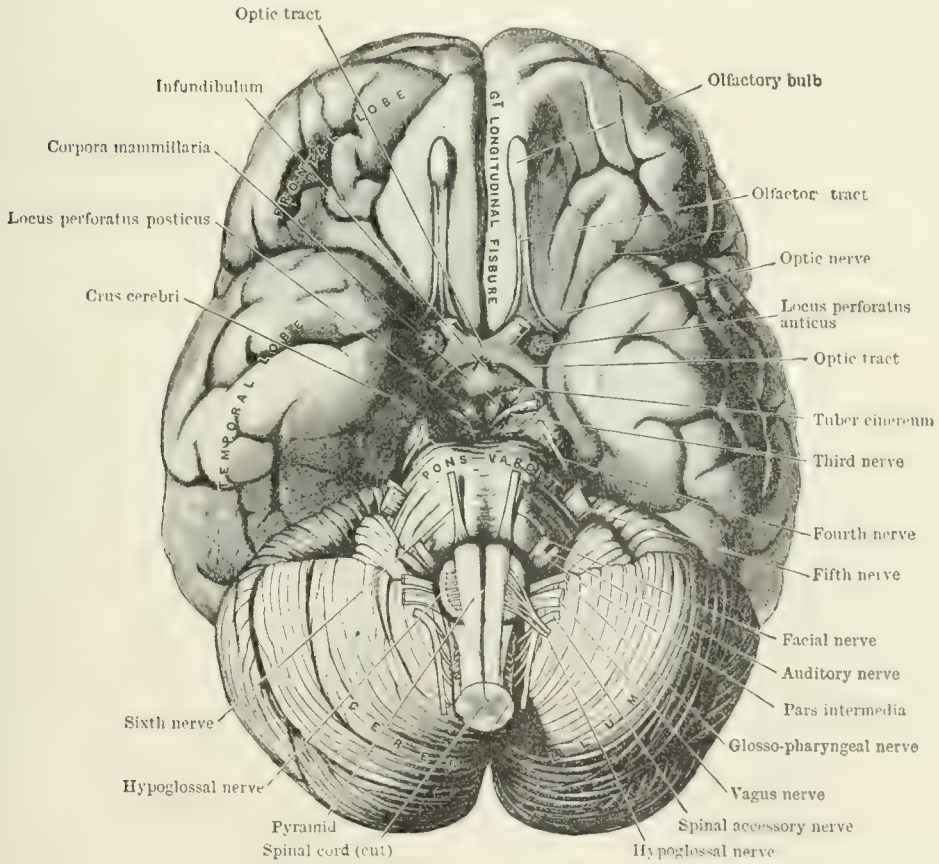

FIG. 901.—The Base of the Brain with the Cranial Nerves Attached. (From Cunningham's Anatomy.)

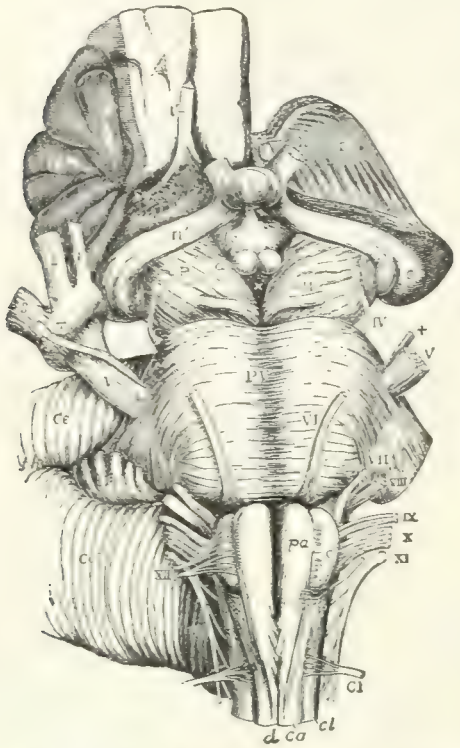

FIG. 902.—The Base of the Brain Stem. *a*, Corpus mamillare; *c*, insula; *ce*, ventral funiculus of spinal cord; *ca*, cerebellum; *cl*, lateral funiculus of spinal cord; *c1*, first cervical nerve; *d*, ventral fissure of spinal cord; *e*, lateral geniculate body; *fl*, flocculus; *h*, hypophysis; *i*, medial geniculate body; *o*, olive; *P*, crus cerebri; *pa*, pyramis; *PV*, pons; *ta*, tuber cinereum; *TA*, thalamus; *I-XII*, cerebral nerves. (From Quain's Anatomy.)

The side walls and floor of the fourth ventricle contain the nuclei of the V. to XII. cerebral nerves, various correlation tissues connected with these nuclei and long conduction paths, like the lemniscus and pyramidal tract, which pass through the oblongata to more distant structures. The cerebellar peduncles rise up from the middle part of the walls of the ventricle and

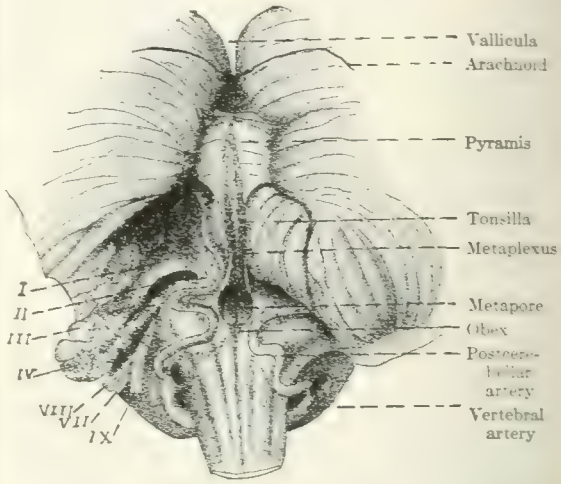

FIG. 904.—The Metapore (Foramen of Magendie) and Adjacent Parts. The left tonsilla of the cerebellum has been removed to expose the underlying parts. *Cf*, Fig. 141. *I*, Velum medullare posterius; *II*, lateral recess of the fourth ventricle; *III*, flocculus; *IV*, plexus chorioideus lateralis; *VII*, *VIII*, *IX*, cerebral nerves. (After Henle and Wilder.)

the cerebellum itself overlaps practically all of the medulla oblongata.

The roof of the fourth ventricle is formed, in its middle part, by the cerebellum. The anterior portion of the roof is a thin sheet of nervous substance, the anterior medullary velum, which stretches between

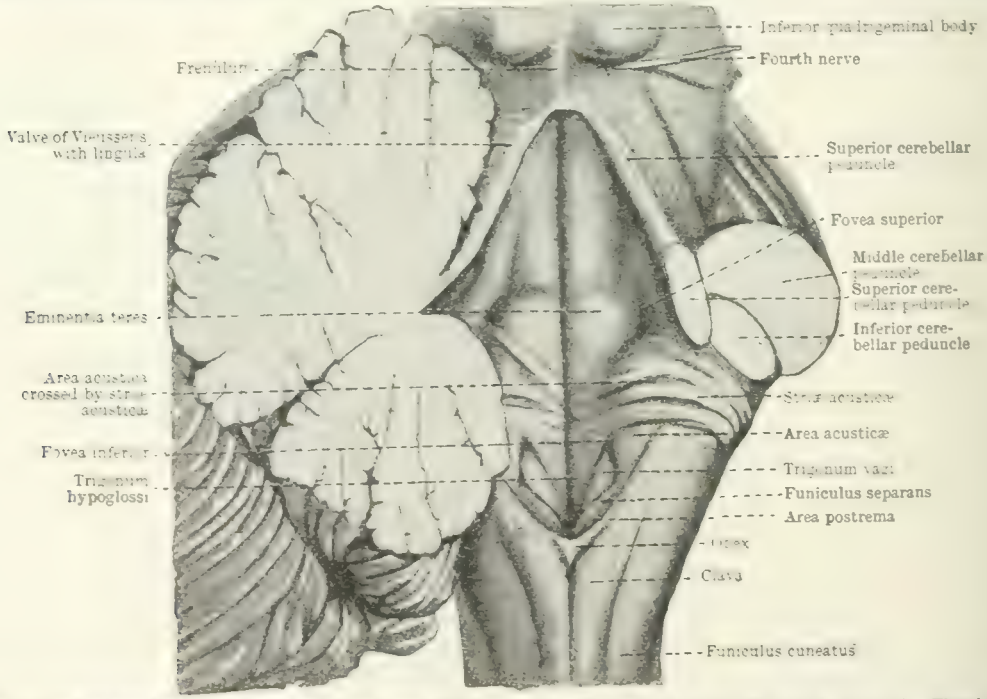

FIG. 903.—The Medulla Oblongata seen from above with the Membranous Roof of the Fourth Ventricle removed. The right half of the cerebellum has been cut away and the left half has been drawn over to the left so as to expose the floor of the fourth ventricle. (From Cunningham's Anatomy.)

the cerebellum and the superior cerebellar peduncles. This velum contains a tract of nerve fibers passing between the roof of the midbrain and the cerebellum, the tractus tecto-cerebellaris, a connection which has long been known in lower vertebrates, but has only recently been discovered in mammals (Edinger). The lower portion of the roof of the fourth ventricle includes the inferior medullary velum, which borders the cerebellum, and a non-nervous tela chorioidea. In the lower part of the tela chorioidea of the fourth ventricle in the adult brain is an opening, the metapore or foramen of Magendie, by which the cavity of the ventricle communicates with the subarachnoid

of figures from the older authors and has added many new figures (vol. ii., Taf. 35, 36, 40) illustrative of the great variability of these structures. Fig. 905 illustrates some features of the superficial anatomy of this region, upon which the underlying nuclei of the cerebral nerves have been projected. The motor nuclei are shown on the left and the sensory nuclei on the right. The superior and inferior foveæ (cf. Fig. 903) probably represent persistent portions of the sulcus limitans, separating in the floor of the ventricle a medial series of motor nuclei (motor VI. nucleus, hypoglossus nucleus and the dorsal motor nucleus under the trigonum vagi) from a lateral series of sensory

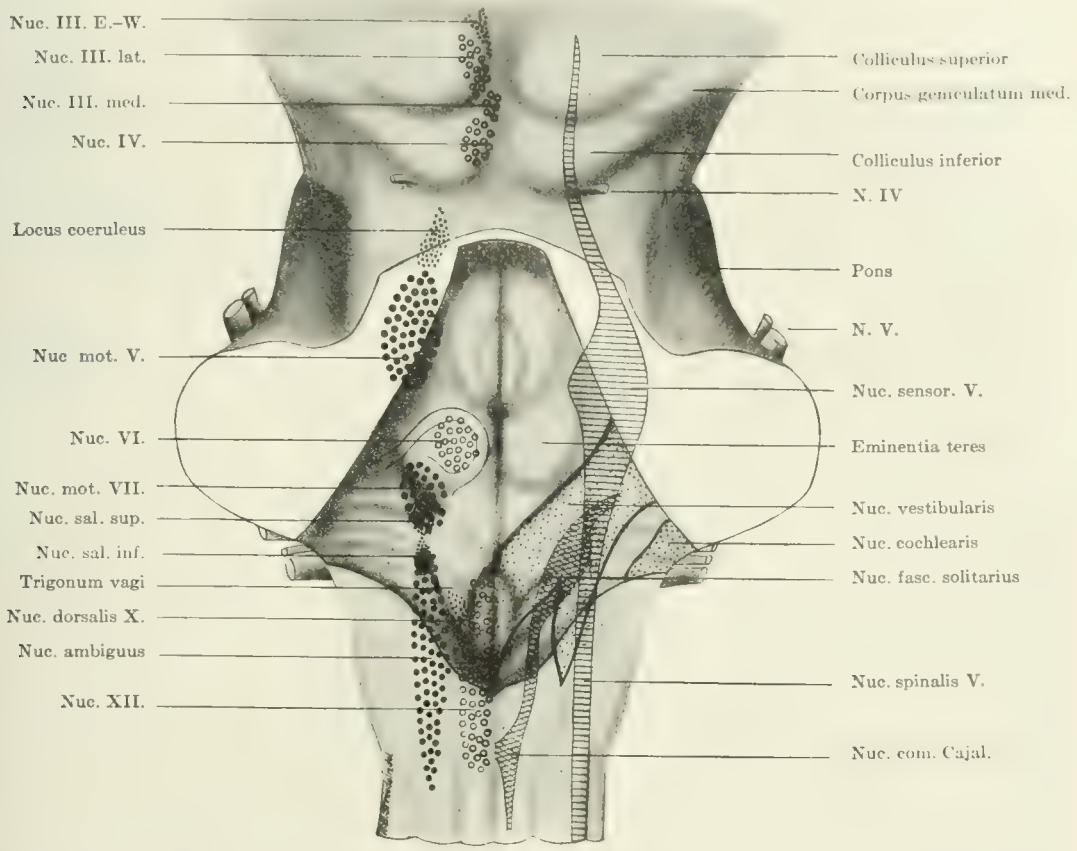

Fig. 905.—Dorsal View of the Human Medulla Oblongata, after the Removal of the Cerebellum and the Roof of the Fourth Ventricle, with the Positions of the Cerebral Nerve Nuclei projected upon the Surface, after the Researches of Streeter, Sabin and others. The motor nuclei are indicated on the left side and the sensory nuclei on the right. *Cf*, Fig. 903. *n. IV*, nervus trochlearis; *n.V.* nervus trigeminus; *nuc. com. Cajal*, the commissural nucleus of Ramón y Cajal; *nuc. III E.–W*, the small-celled or visceral motor nucleus of the III nerve, or nucleus of Edinger-Westphal; *nuc. III lat.*, lateral nucleus of III nerve; *nuc. III med.*, medial nucleus of the III nerve; *nuc. mot. VII*, chief motor nucleus of the VII nerve; *nuc. sal. inf.*, nucleus salivatorius inferior; *nuc. sal. sup.*, nucleus salivatorius superior.

space (Fig. 904). Blake has shown that in cats and dogs there is a sac-like protrusion of the plexus in this place, and that in man and apes the larger part of the sac disappears, leaving a free opening. The membranous wall of the lateral recesses of the fourth ventricle likewise is interrupted, allowing a free communication between the cavities of these recesses and the subarachnoid space. These are the foramina of Luschka. See the section on the *Meninges*, beyond.

The floor of the fourth ventricle is marked by a complex series of eminences and depressions which have been variously and often erroneously described. Retzius (1896, vol. i., p. 41) has reproduced a number

nuclei. In the portion of the rhomboidal fossa which lies between the superior and inferior foveæ the sulcus limitans is more or less completely obliterated by the overlapping vestibular nuclei and striæ medullares acusticæ. But the form of these striæ is exceedingly variable and in some brains the sulcus limitans is not interrupted by them. The motor V., motor VII., and the nucleus ambiguus lie farther from the ventricular surface and father laterally than the motor VI. and XII. nuclei and the trigonum vagi, and hence do not influence the ventricular sculpture as they do in lower brains. The ventrolateral position of these motor nuclei has been secondarily acquired in the

course of evolutionary history, for they lie close to the ventricular surface in fishes (cf. Figs. 883 and 884). The relations of the structures here figured and of other internal organs of the medulla oblongata can be seen in the cross-section pictures shown in Figs. 906 to 919.

As shown by Figs. 905 and 884, the motor nuclei of the brain stem are arranged in medial and lateral columns (cf. also Fig. 889, illustrating the superficial origins of the medial and lateral motor roots). The former, or somatic motor series, includes the III., IV., VI. and XII. nuclei. The latter, or visceral motor series, includes the visceral motor component of the III. nucleus for the ciliary ganglion, the motor V., the chief motor VII., the superior and inferior salivatory nuclei, the dorsal motor nucleus of the IX. and X. and the nucleus ambiguus. Similarly the sensory nuclei are arranged in two series, though this is less evident in the adult brain than in the embryo and the lower vertebrates. The ventromedial series is visceral sensory and gustatory in function and comprises the nucleus of the fasciculus solitarius and the associated gray centers. It receives the portio intermedia of the facial nerve and the visceral sensory (including gustatory) roots of the IX. and X. nerves. The dorsal sensory nucleus of the IX. and X. nerves is simply an enlargement of the nucleus of the fasciculus solitarius (Ramón y Cajal). The somatic sensory nuclei are more dorsal and lateral and comprise the sensory V. nuclei, including the mesencephalic nucleus and the substantia gelatinosa of Rolando, and the VIII. nuclei.

We have already seen that the analysis of the cerebral centers into visceral and somatic reflex systems is primitive and fundamental. The visceral systems typically reach their peripheral distribution through the sympathetic nervous system; but in the cerebral nerves certain highly specialized components of visceral type are entirely distinct from the sympathetic system. The visceral components of the cerebral nerves, therefore, belong to two general classes. First, there are the unspecialized visceral components which, like those of the spinal nerves, distribute peripherally through the sympathetic system. Here belong the preganglionic sympathetic efferent neurones of the III. nerve for the ciliary ganglion, the salivatory and other efferent sympathetic neurones of the VII., IX., X. and XI. nerves; also some general visceral afferent fibers entering the nuclei associated with the fasciculus solitarius from mucous surfaces and viscera. In the second class are some very highly specialized components of the cerebral nerves which clearly belong to the visceral systems. Chief of these are the motor nerves from the ventrolateral series of motor nuclei of the oblongata (V., VII., IX., X., XI. nerves) for striated muscles. These muscles are believed upon comparative and embryological grounds to be derived from the gill muscles of fishes and, embryologically, from the visceral or splanchnic mesoderm, rather than from the somites which give rise to the skeletal muscles and the eye muscles. Their motor nerves resemble in anatomical and physiological characteristics those of the somatic motor series and are believed to have become differentiated away from other visceral motor nerves (by the suppression of the postganglionic neurone, etc.) as a physiological adaptation. Their connection with the lateral series of motor nuclei, however, gives the clue to their evolutionary origin. The gustatory system is similarly believed to have been derived as a specialization from the general visceral sensory system, and its peripheral nerve fibers all terminate in the nuclei associated with the fasciculus solitarius in company with those of the unspecialized visceral sensory system.

The primary centers for the cerebral nerves in the brain stem may, therefore, be classified as follows:

Somatic efferent (III, IV, VI, XII.)
Visceral efferent.
- Unspecialized systems, giving rise to preganglionic sympathetic fibers (nucleus of ciliary branches of III. nerve, nuclei salivatorii of VII. and IX. nerves, dorsal motor nucleus of X.)
- Specialized systems, for striated (branchiomeric) visceral muscles, forming the ventrolateral motor nuclei (chief motor V. and VII., nucleus ambiguus).

Visceral sensory, terminating in the nucleus of the fasciculus solitarius and dorsal sensory nucleus of IX. and X.
- Unspecialized systems (visceral sensory fibers entering the VII., IX., and X. nerves from the sympathetic system).
- Specialized systems (gustatory fibers from the VII. and IX. nerves—also from the X. nerve in lower vertebrates.)

Somatic sensory.
- Cutaneous nerves and nerves of general sensibility from mucous lining of mouth and tongue (V., IX., X.)
- Nerves of deep sensibility—muscle sense, joint sense, etc. (muscle sense of eye muscles, in III., IV., and VI. nerves, cerebral center unknown; muscle sense of other cephalic muscles in V. nerve, cerebral center probably in mesencephalic nucleus of V. nerve.)
- Vestibular nerve.
- Cochlear nerve.

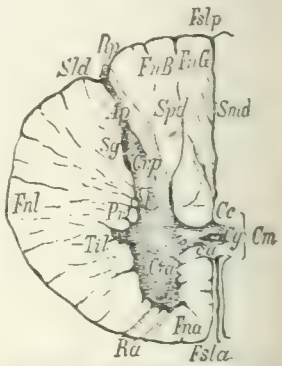

Fig. 906.—Cross Section through the Human Spinal Cord, stained with Carmine. (After H. Obersteiner, "Anleitung beim Studium des Baues der nervösen Centralorgane im gesunden und kranken Zustande," iii. Aufl., Leipzig und Wien, 1896, S. 227, Fig. 96. Transverse section at the level of C iii; *Cc*, commissura grisea; *Ap*, apex columnæ dorsalis; *Ca*, commissura ventralis alba; *Cc*, canalis centralis; *Cm*, commissura medullæ spinalis; *Cra*, cornu ventralis; *Crp*, cornu dorsalis; *Fna*, funiculus ventralis; *FnB*, fasciculus cuneatus Burdachi; *FnG*, fasciculus gracilis Golli; *Fnl*, funiculus lateralis; *Fsla*, fissura mediana ventralis; *Fslp*, sulcus medianus dorsalis; *k*, tractus solitarius; *Pr*, formatio reticularis; *Ra*, radix ventralis; *Rp*, radix dorsalis; *Sg*, substantia gelatinosa Rolandi; *Sld*, sulcus lateralis dorsalis; *Smd*, septum medianum dorsale; *Spd*, septum intermedium dorsale; *Tvl*, tractus intermedio lateralis.

The Brain Stem, Cross-sections.—Let us next examine a series of cross-sections through the brain stem, in which the relations of these centers are revealed in detail, after which the cerebral nerves will be reviewed in sequence.

The general topography of the spinal cord in the midcervical region is shown in Fig 906.

A little higher up, just at the junction of the cervical spinal cord with the medulla oblongata, the relations of the gray matter to the white matter change considerably. In Fig. 907 one can easily make out that the gray matter is more abundant than at the lower level, that the dorsal horns of gray matter are inclined much more lateralward instead of dorsalward, while the neck of gray matter connecting the dorsal horn with the rest of the gray matter is very long and narrow. In the region of the lateral horn of gray matter the white and gray matter are much mixed up, corresponding to the beginning of the formatio reticularis of the medulla oblongata.

A section taken through one side of the central nervous system of the new-born babe at the junction of the cervical portion of the spinal cord with the

medulla oblongata will show certain particulars not brought out in previous sections (see Fig. 908). Here not all the white matter is medullated. Thus,

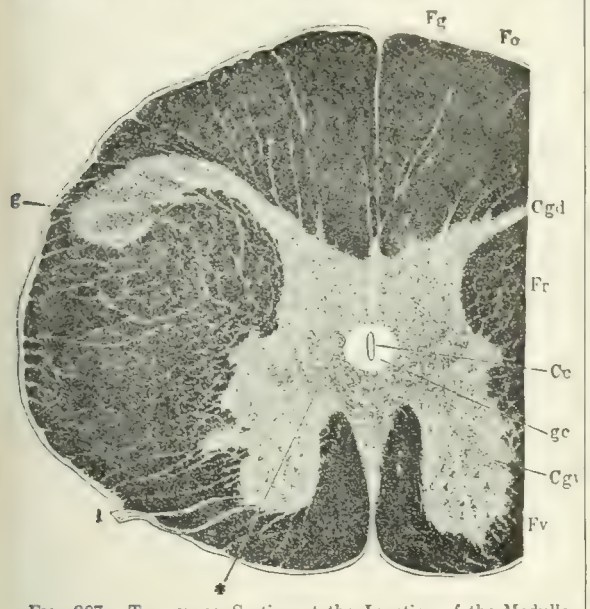

Fig. 907.—Transverse Section at the Junction of the Medulla Spinalis with the Medulla Oblongata. (After J. Henle, "Handbuch der Nervenlehre des Menschen," zweite Aufl., Braunschweig, 1879, S. 208, Fig. 124.) *Cc*, Canalis centralis; *Cpl*, columna (grisea) dorsalis; *Cgv*, columna (grisea) ventralis; *Fv*, funiculus ventralis; *Fc*, fasciculus cuneatus; *Fg*, fasciculus gracilis; *g*, substantia gelatinosa Rolandi; *gc*, substantia gelatinosa centralis; *I*, ventral root of the first cervical nerve; the asterisk * indicates a cross section of a blood-vessel; *Fr*, formatio reticularis. This section is below the level of the decussatio pyramidum.

for example, the fibers of the pyramidal tract are not yet surrounded by myelin sheaths. In the center is seen the *canalis centralis;* ventral from it is a white area corresponding to the non-medullated

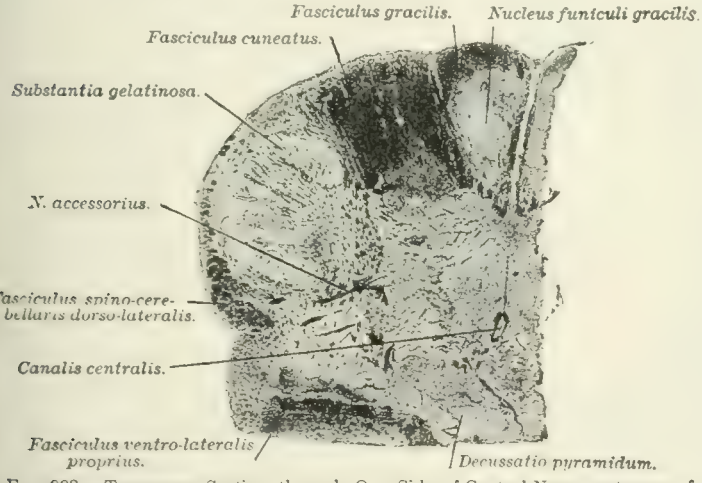

Fig. 908.—Transverse Section through One Side of Central Nervous System of New-born Babe at Junction of Pars Cervicalis Medullæ Spinalis with the Medulla Oblongata, Showing the N. Accessorius. (Weigert-Pal preparation by Dr. John Hewetson, drawing by A. Karsted.) (From "The Nervous System and Its Constituent Neurones," New York, D. Appleton & Co., 1899.)

decussation of the pyramids (*decussatio pyramidum*); dorsal from the central canal is a mass of gray matter and a medial dorsal septum and sulcus. The ventral part of the section has been cut off so that the gray matter of the ventral horn is not well shown. That of the dorsal horn is, however, well illustrated. It is directed, however, far lateralward instead of

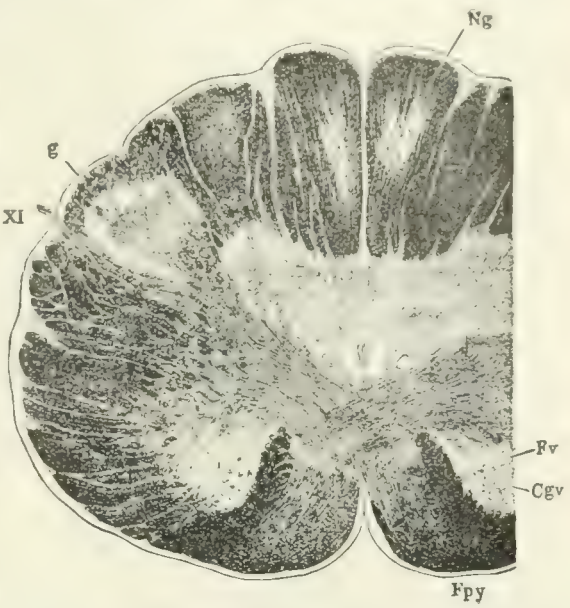

Fig. 909.—Transverse Section through the Medulla Oblongata at the Level of the Decussatio Pyramidum. (After J. Henle, "Handbuch der Nervenlehre des Menschen," Zweite Aufl., Braunschweig, 1879, S. 211, Fig. 126.) *Cgv*, Columna (grisea) ventralis or ventral horn; *Fv'*, continuation in the medulla of the fasciculus ventralis proprius (*Vorderstrangrest* of the Germans); *Fpy*, fasciculi cerebro-spinales pyramidales undergoing decussation; *g*, substantia gelatinosa Rolandi; *Ng*, spinal extremity of nucleus funiculi gracilis; *XI*, nervus accessorius.

backward, and is capped by a large mass of gelatinous substance (*substantia gelatinosa Rolandi*). Between the dorsal horn and the median line are two new masses of gray matter not met with in the spinal cord lower down; one very well developed, occupying a large part of the region of the funiculus gracilis, is called the *nucleus funiculi gracilis* or Goll's nucleus. Lateral from it, in the ventral part of the fasciculus cuneatus, a mass of gray matter is beginning to appear which higher up becomes very voluminous and is known as the *nucleus funiculi cuneati* or Burdach's nucleus. The white matter surrounds the gray matter, as before, and is again divisible into the funiculus ventralis, the funiculus lateralis, and the funiculus dorsalis. The funiculus ventralis includes the non-medullated pyramid and the partly medullated fasciculus ventralis proprius. The funiculus lateralis includes the partially medullated fasciculus ventralis proprius, the well-medullated fasciculus spino-cerebellaris dorso-lateralis. In the funiculus dorsalis are seen the well-medullated fasciculus gracilis and the well-medullated fasciculus cuneatus. Passing transversely lateralward through the gray matter and through the funiculus lateralis are seen the root fibers of the accessory nerve (*radix nervi accessorii*). A good deal of white matter mixed up with gray matter is visible in the lateral region. This corresponds to the beginning of the *formatio reticularis.* A section from a similar region in the adult is shown in Fig. 909. In

this figure the decussation of the pyramids is well marked.

At a little higher level (Fig. 910), the relations of the gray matter to the white matter have become still more complex. The fasciculus gracilis is almost entirely replaced by the nucleus funiculi gracilis, and the funiculus cuneatus is much encroached upon by the nucleus funiculi cuneati. The region of the lateral funiculus is being converted largely into a mass of formatio reticularis. The substantia gelatinosa Rolandi has increased in bulk, and between it and the surface lie, instead of the fasciculus of Lissauer met with in the spinal cord, the descending fibres of the spinal tract of the trigeminal nerve (*tractus spinalis nervi trigemini*).

In a section at a higher level (Fig. 911) the central canal has opened out into the lower part of the fourth ventricle. Below the stratum griseum centrale is the nucleus nervi hypoglossi (**24**). Just dorsad from this nucleus is situated part of the nucleus alæ cinereæ (**22**), while more laterally and dorsally placed is seen the upward continuation of the nucleus funiculi gracilis (**19, 23**); some fibers of the funiculus gracilis are still present (**20**). Still more lateralward is seen the upward continuation of the funiculus cuneatus (**16**), and ventrad from this the nucleus funiculi cuneati (**17, 25**). Curving around the funiculus cuneatus are a few of the fibræ arcuatæ superficiales dorsales. More ventrally situated is the corpus restiforme (**12**), here consisting chiefly of the upward continuation of the direct cerebellar tract from the spinal cord. The pale mass of substantia gelatinosa is visible at **13**, while lateralward from it are seen in transverse section the descending fibers of the tractus spinalis nervi trigemini (**11**). Just lateralward from this are more lateral superficial arcuate fibers (**10**); ventralward from the substantia gelatinosa are situated the nuclei laterales (**8, 29**). In the zone between

Fig. 911.—Transverse Section through the Medulla Oblongata in the Region of the Distal Portion of the Fossa Rhomboidea of an Adult Human Being. The Nerve fibers have been drawn in on the left side (Weigert-Wolters' staining); on the right side, the cells (Nissl's stain). (After E. Flatau, "Atlas Cerebri Humani," Tab. x., Fig. B.) 1, Fissura longitudinalis mediana; 2, stratum interolivare lemnisci; 3, pyramis; 4, radix nervi hypoglossi; 5, nucleus olivaris inferior; 6, fibræ arcuatæ superficiales laterales; 7, nucleus olivaris accessorius dorsalis; 8, nucleus lateralis; 9, substantia reticularis grisea with fibræ arcuatæ internæ; 10, fibræ arcuatæ superficiales laterales; 11, tractus spinalis nervi trigemini 12, corpus restiforme; 13, substantia gelatinosa; 14, nervus hypoglossus; 15, fibræ arcuatæ superficiales dorsales; 16, funiculus cuneatus Burdachi; 17, nucleus funiculi cuneati; 18, tractus solitarius; 19, nucleus funiculi gracilis; 20, funiculus gracilis Golli; 21, distal part of fossa rhomboidea; 22, nucleus alæ cinereæ; 23, nucleus funiculi gracilis; 24, nucleus nervi hypoglossi; 25, nucleus funiculi cuneati; 26, scattered cells of the formatio reticularis grisea; 27, substantia gelatinosa; 28, dorsal part of substantia reticularis alba (fasciculus longitudinalis medialis); 29, nucleus lateralis; 30, cells of the nucleus olivaris accessorius dorsalis; 31, cells of the nucleus olivaris inferior; 32, raphe with the stratum interolivare lemnisci on each side of it. On both sides of the raphe lie some scattered small cells; 33, cells of the nuclei arcuati. Some large cells which lie in the region between the dorsal accessory olive (30) and the substantia gelatinosa (27) belong to the nucleus ambiguus.

Fig. 910.—Transverse Section through the Medulla Oblongata at the Level of the Most Caudal Fila Radicularia of the Nervus Hypoglossus. (After J. Henle, "Handbuch der Nervenlehre des Menschen," Zweite Aufl., Braunschweig, 1879, S. 213, Fig. 127.) *Fv*, Continuation in the Medulla of the fasciculus ventralis proprius of the spinal cord; *Fpy*, pyramis (at uppermost level of decussatio pyramidum); *g*, substantia gelatinosa; *Nc*, nucleus funiculi cuneati (Burdachi); *Ng*, nucleus funiculi gracilis (Golli). The decussatio lemniscorum is not indicated in the figure, though it is to be seen at this level.

the area above described and the radix n. hypoglossi (**4, 14**) are seen the following structures: the tractus solitarius (**18**), which represents chiefly descending fibers from the nervus glosso-pharyngeus, the formatio reticularis with many fibræ arcuatæ internæ (**9**), the nucleus olivaris accessorius dorsalis (**7, 30**), the nucleus olivaris inferior (**5, 31**), and the fibræ arcuatæ superficiales laterales (**6**). In the middle line is seen the raphe extending from the fissura longitudinalis ventralis (**1**) to the floor of the fourth ventricle (**21**). From the dorsal surface ventralward between the raphe and the radix n. hypoglossi the following structures are met with: Below the gray matter are seen in transverse section the fibers of the fasciculus longitudinalis medialis. Ventral from this are the transverse sections of the fibers of the stratum interolivare lemnisci which are made up of internal arcuate fibers which have crossed the raphe and turned to run longitudinally. Among these fibers some small cells are present (**32**). At the most ventral part of the interolivary layer of the lemniscus are seen many transverse fibers; at the level of the olive

Fig. 912.—Transverse Section through the Medulla Oblongata in the Region of the Nucleus Nervi Hypoglossi and Nucleus Alæ Cinereæ in an Adult Human Being. On the left side the fibers are photographed (Weigert-Wolters' stain); on the right side the cells have been drawn in from Nissl preparations. (After E. Flatau, "Atlas Cerebri Humani," Tab. xi., Fig. A.) 1, Stratum interolivare lemnisci; 2, fibræ arcuatæ superficiales ventrales; 3, nuclei arcuati; 4, pyramis; 5, fibræ arcuatæ superficiales lateralis; 6, nucleus olivaris inferior; 7, nucleus olivaris accessorius dorsalis; 8 and 9, fibræ arcuatæ internæ; 10, tractus spinalis nervi trigemini; 11, nervus vagus; 12, corpus restiforme; 13, nucleus funiculi cuneati; 14, remains of the nucleus funiculi gracilis and bundles of the radix descendens nervi vestibuli; 15, tractus solitarius; 16, nucleus alæ cinereæ; 17, formatio reticularis grisea; 18, nervus hypoglossus; 19, nucleus nervi hypoglossic; 20, raphe; 21, nucleus nervi hypoglossi; 22, nucleus nervi vagi; 23, nucleus nervi vestibuli; 24, groups of cells which belong partly to the nucleus funiculi cuneati and partly to the nucleus tractus solitarii; 25, nucleus funiculi cuneati; 26, scattered cells in the formatio reticularis grisea; 27, cells of the substantia gelatinosa; 28, cells of the nucleus lateralis; 29, cells of the nucleus ambiguus; 30, cells of the nucleus lateralis; 31, cells of the nucleus olivaris accessorius dorsalis; 32, cells of the nucleus olivaris inferior; 33, cells of the nucleus arcuati; 34 and 35, cells of the nucleus olivaris accessorius medialis; 36, nuclei arcuati.

(**2**) the large bundle of white fibers on the ventral surface is the pyramis (**3**). At the periphery of the pyramid a few cells are seen which represent a continuation downward of the nuclei arcuati of the pons.

If a section be taken still higher up the relations become somewhat more complex (see Fig. 912). The fourth ventricle has become much wider, the two halves of the medulla are separated from each other by the raphe (**20**). In the floor of the fourth ventricle, passing from the middle line lateralward, are seen the nucleus n. hypoglossi (**19, 21**), the nucleus alæ cinereæ (**16, 22**), the tractus solitarius (**15**), and the lower portion of the nucleus n. vestibuli (**23**), near which are a few fibers of the fasciculus cuneatus and some fibers of the radix descendens n. vestibuli (**14**). Each half of the medulla is divisible by means of the radix n. vagi and the radix n. hypoglossi into three compartments; one lateral between the dorso-lateral edge and the radix n. vagi, one middle between the radix n. vagi and the radix n. hypoglossi, and one medial between the radix n. hypoglossi and the raphe.

In the lateral compartment can be seen the corpus restiforme (**12**), the nucleus funiculi cuneati (**13, 25**), the tractus spinalis n. trigemini (**10**), and the substantia gelatinosa (**27**).

In the middle compartment there are the fibræ arcuatæ superficiales laterales (**5**), the nucleus olivaris inferior (**6, 32**), the nucleus olivaris accessorius dorsalis (**7, 31**), the fibræ arcuatæ internæ (**8, 9**), the formatio reticularis grisea (**17, 26**), the nuclei laterales (**28**), and the nucleus ambiguus (**29**) which is the chief motor nucleus of origin of the n. vagus and the n. glosso-pharyngeus.

In the medial compartment, passing from the dorsal surface ventralward, is seen the stratum interolivare lemnisci (**1**), the ventral superficial arcuate fibers (**2**), the pyramis (**4**), the nuclei

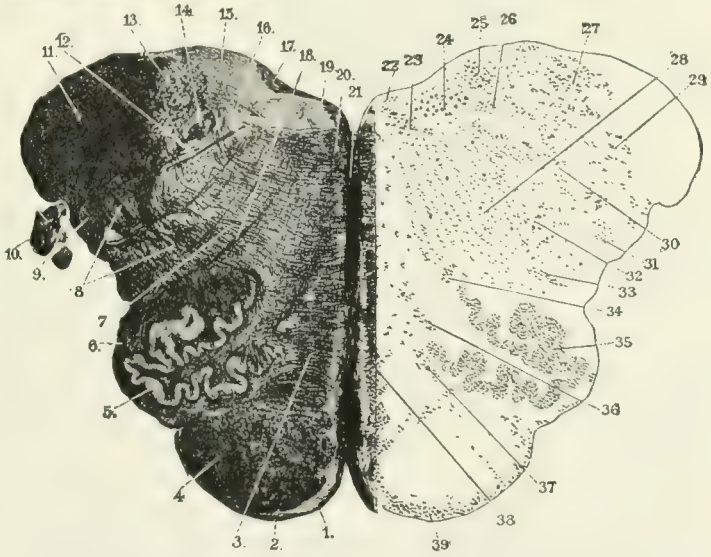

Fig. 913.—Transverse Section through the Medulla Oblongata at the Level of the Nervus Vagus and Nervus Glosso-Pharyngeus in an Adult Human Being. On the left side, photograph of a fiber preparation; on the right side the cells have been drawn in from Nissl preparations. (After E. Flatau, "Atlas Cerebri Humani," Tab. xi., Fig. 13.) 1, Nuclei arcuati; 2, fibræ arcuati superficiales ventrales; 3, stratum interolivare lemnisci; 4, pyramis; 5, nucleus olivaris inferior; 6, fibræ arcuatæ superficiales laterales; 7, formatio reticularis grisea with fibræ arcuatæ internæ; 8, fibræ cerebello-olivares; 9, tractus spinalis nervi trigemini; 10, extramedullary bundle of the nervus vagus and nervus glossopharyngeus; 11, corpus restiforme; 12, bundle of the nervus glossopharyngeus (the radial fibers running medial from this and not lettered represent the motor fibers of the vagus and glosso-pharyngeal nerves); 13, radix descendens nervi vestibuli; 14, tractus solitarius; 15, nucleus nervi vestibuli; 16, nucleus nervi glossopharyngei; 17, striæ medullares; 18, radial fibers in the formatio reticularis grisea (at the boundary between the fibræ arcuatæ internæ and the fibræ cerebello-olivares); 19, nucleus funiculi teretis; 20, fasciculus longitudinalis medialis; 21, raphe; 22, nucleus funiculi teretis; 23, cells which lie dorsalward from the fasciculus longitudinalis medialis and belong to the cells of the formatio reticularis grisea; 24, nucleus nervi vagi; 25, nucleus nervi vestibuli medialis; 26, nucleus nervi glosso-pharyngei; 27, cells of the nucleus nervi vestibuli lateralis (Deiters) and of the remains of the dorsal horn of the spinal cord; 28, scattered cells of the formatio reticularis grisea; 29, cells belonging to 27; 30, cells of the substantia gelatinosa; 31, nucleus lateralis; 32, cells of the nucleus ambiguus; 33, nucleus lateralis (?); 34, cells of the nucleus olivaris accessorius dorsalis; 35, 36, 37, cells of the nucleus olivaris inferior; 38, 39 cells of the nuclei arcuati.

arcuati (**3**), and the nucleus olivaris accessorius medialis (**34, 35**).

In the next section (Fig. 913), taken from the upper part of the medulla oblongata, the fourth ventricle is very wide and the corpus restiforme has become very markedly developed. In the floor of the fourth ventricle, passing from the middle line lateralward, are seen the nucleus funiculi teretis (**19, 22**), the nucleus alæ cinereæ (**24**), the striæ medullares or striæ acustici (**17**), the nucleus n. vestibuli medialis (**15, 25**). The corpus restiforme (**11**) is seen as a large mass of fibers cut transversely at the lateral dorsal angle of the cross-section. Just medial to it are seen the bundles of the radix descendens n. vestibuli (**13**). In many of these bundles are masses of gray matter (**27**) which represent chiefly the nuclei of the descending root of the vestibular nerve. The round bundle formed by the tractus solitarius (**14**) is clearly visible, and close to it the nucleus tractus solitarii (**26**); at **9** the tractus spinalis n. trigemini is seen crossed by black bundles of fibers, the fibræ cerebello-olivares (**8**). Medial from the tractus spinalis n. trigemini are situated the cells of the substantia gelatinosa (**30**). The nucleus lateralis (**31**) is still visible. The motor nucleus of the n. vagus and of the n. glosso-pharyngeus; or so-called nucleus ambiguus, is visible. At this level (**33**) the fibræ arcuatæ internæ (**7**) are numerous, crossing the formatio reticularis grisea and running toward the raphe.

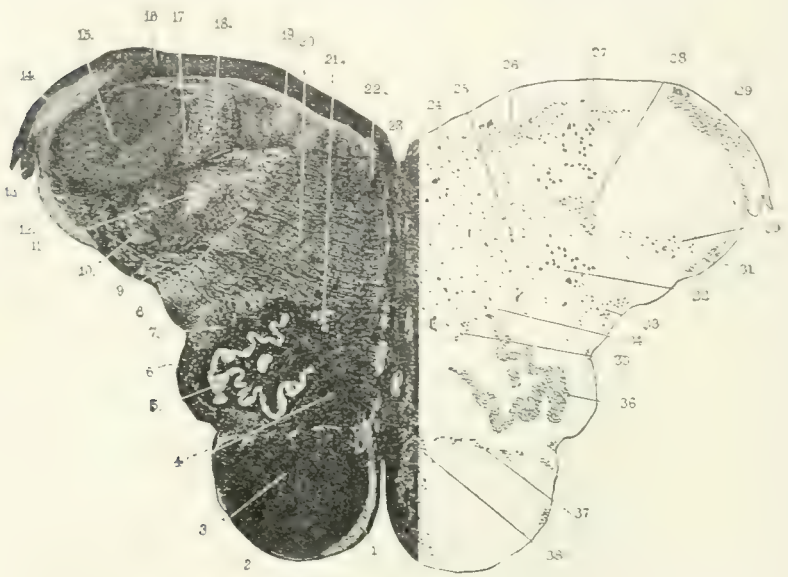

FIG. 914.—Transverse Section through the Proximal Part of the Medulla Oblongata at the Region of Entrance of the Nervus Acusticus in an Adult Human Being. On the left the fibers have been photographed; on the right the cells have been drawn in. (After E. Flatau, "Atlas Cerebri Humani," Tab. xii., Fig. A.) 1, Nuclei arcuati; 2, fibræ arcuatæ superficiales ventrales; 3, pyramis; 4, stratum interolivare lemnisci; 5, nucleus olivaris inferior; 6, fibræ arcuatæ superficiales laterales; 7, fasciculus tegmenti centralis, or centrale Haubenbahn of von Bechterew; 8, fibræ arcuatæ internæ; 9, fibræ cerebello-olivares; 10, tractus spinalis nervi trigemini; 11, substantia gelatinosa; 12, nucleus nervi cochleæ ventralis; 13, nervus cochleæ; 14, nucleus nervi cochleæ dorsalis (tuberculum acusticum); 15, corpus restiforme; 16, striæ medullares (very markedly developed); 17, radix nervi glosso-pharyngei; 18, radix descendens nervi vestibuli; 19, nucleus nervi vestibuli medialis; 20, formatio reticularis grisea; 21, stratum interolivare lemnisci; 22, fasciculus longitudinalis medialis; 23, raphe; 24, cells dorsal from the fasciculus longitudinalis medialis connected with the nucleus reticularis tegmenti; 25, scattered cells of the tegmentum (von Bechterew's nucleus reticularis tegmenti); 26, nucleus nervi vestibuli medialis; 27, nucleus nervi vestibuli lateralis (Deiters); 28, cells of the substantia gelatinosa; 29, cells of the tuberculum acusticum; 30, tongue-like collection of cells; 31, ventro-medial continuation of the nucleus nervi cochleæ ventralis; 32, nucleus nervi facialis; 33, nucleus lateralis; 34, large multipolar cells (connected with the scattered cells of the formatio reticularis grisea); 35, nucleus olivaris accessorius dorsalis; 36, cells of nucleus olivaris inferior; 37, scattered cells at the dorsal periphery of the pyramid (beginning nuclei pontis); 38, cells of the nuclei arcuati.

The nucleus olivaris inferior (**5, 35**) is accompanied by the nucleus olivaris accessorius dorsalis (**34**) and the nucleus olivaris accessorius medialis (**37**). Dorso-lateral from the olive are the fibræ arcuatæ superficiales laterales. In the middle line is seen the raphe and close to it the fasciculus longitudinalis medialis (**20**), the stratum interolivare lemnisci (**3**), and the pyramis (**4**); running around the pyramid are the fibræ arcuatæ superficiales ventrales (**2**), and the nuclei arcuati (**1, 38, 39**).

The section which follows (Fig. 914) is taken at the uppermost part of the medulla oblongata just where it goes over into the pons. Here the fourth ventricle is at its widest, and running transversely across it are seen the striæ medullares (**16**). Connected lateralward with the nucleus n. cochleæ dorsalis or tuberculum acusticum (**14**) is the n. cochleæ. In the floor of the fourth ventricle, passing from the middle line lateralward, can be seen some cells of the nucleus reticularis tegmenti (**24**) and the nucleus n. vestibuli medialis (**19, 26**). The corpus restiforme (**15**) is separated from the periphery by the dorsal cochlear nucleus (**14, 29**); medial from it the radix descendens n. vestibuli is present in the form of numerous discrete bundles in among which are situated the large multipolar ganglion cells of Deiters' nucleus (nucleus n. vestibuli lateralis) (**27**). Ventral from the corpus restiforme and the radix descendens n. vestibuli are seen the root fibers of the n. glosso-pharyngeus (**17**). A portion of the nucleus n. cochleæ ventralis is visible (**12, 31**). Ventralward from the root fibers of the glosso-pharyngeal nerve are seen the fibers of the tractus spinalis n. trigemini (**10**), and medial from them the cells of the substantia gelatinosa (**11, 28**). The formatio reticularis (**20**) is well developed. It is crossed as in the sections below by many fibræ arcuatæ internæ (**8**); the fibræ cerebello-olivares are still visible (**9**). The section passes through the upper part of the nucleus olivaris inferior (**5**) and a portion of the nucleus olivaris accessorius dorsalis (**21, 35**). The fibræ arcuatæ superficiales laterales are still present (**6**), and dorso-lateral from the olive are seen some of the fibers of the fasciculus tegmenti centralis or centrale Haubenbahn of von Bechterew (**7**). A good many fibers run longitudinally in the raphe (**23**). The fasciculus longitudinalis medialis (**22**) is larger than in the sections below. The stratum interolivare lemnisci (**4**) is highly developed just before going over into the lemniscus medialis of the pons. The pyramis (**3**) is large, is surrounded by the fibræ arcuatæ superficiales ventrales, and has close to it the nuclei arcuati (**1, 38**).

In sections through the pons we have to distinguish between the pars dorsalis pontis and the pars basilaris pontis. The pars basilaris pontis includes the large fasciculi longitudinales of the pons, the large bundles of transverse fibers of the pons, and the great gray masses known as the nuclei pontis. The pars dorsalis pontis includes the upward continuation of the medulla oblongata with the exception of the pyramids. It

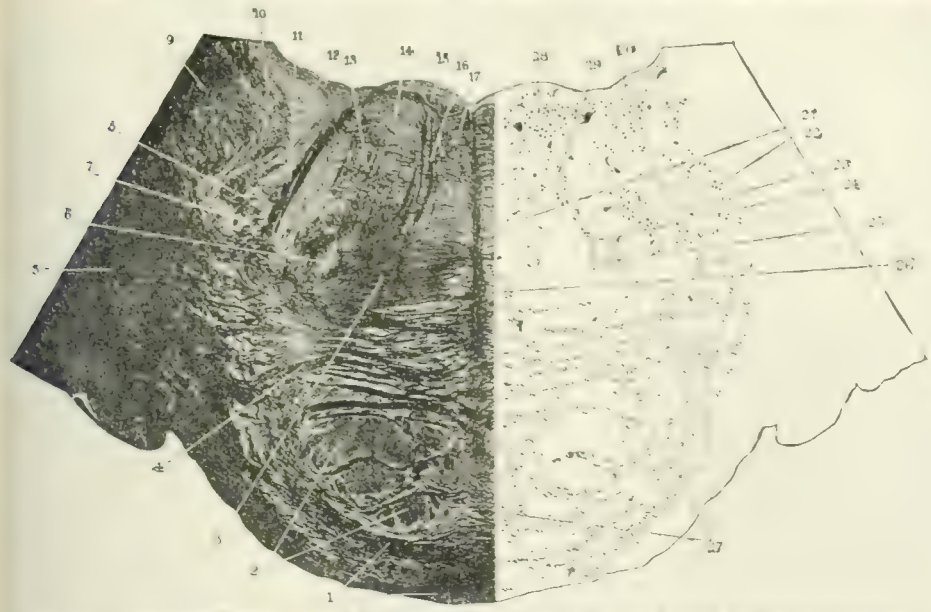

FIG. 915.—Transverse Section through the Pons at the Level of the Nervus Facialis and Nervus Abducens in an Adult Man. On the left side the fibers have been photographed; on the right the cells have been drawn in. (After E. Flatau, "Atlas Cerebri Humani," Berlin, 1899, Tab. xii., Fig. B.) 1, Fibræ pontis superficiales; 2, fasciculi longitudinales pontis; 3, lemniscus medialis; 4, fibræ pontis profundæ; 5, brachium pontis; 6, nucleus olivaris superior; 7, substantia gelatinosa (beginning sensory nucleus of the trigeminus); 8, tractus spinalis nervi trigemini; 9, corpus restiforme (ascending to cerebellum); 10, radix descendens nervi vestibuli; 11, radix nervi facialis pars secunda; 12, nucleus nervi vestibuli medialis; 13, formatio reticularis grisea with ascending fibers from the nucleus nervi facialis and fibers from the nucleus olivaris superior to the nucleus nervi abducentis; 14, nucleus nervi abducentis; 15, genu internum nervi facialis; 16, nervus abducens; 17, fasciculus longitudinalis medialis; 18, nucleus nervi abducentis; 19, cells of formatio reticularis grisea; 20, nucleus nervi vestibuli lateralis Deiters; 21, nucleus reticularis tegmenti von Bechterew; 22, cells of the substantia gelatinosa; 23, cells of the proximal part of the nucleus nervi facialis or of the distal motor nucleus of the nervus trigeminus; 24 and 25, cells of the nucleus olivaris superior; 26, continuation of the nuclei pontis in the tegmentum; 27, nuclei pontis.

facialis and the n. abducens. In the pars dorsalis pontis the raphe is seen in the middle line. The nucleus n. abducentis is situated close to the floor of the fourth ventricle (**14, 18**). Running ventralward from the medial side of the nucleus are seen the root fibers of the n. abducens (**16**); the nucleus n. facialis is present (**23**); the pars prima of the radix n. facialis exists as a number of scattered fibers radiating dorsalward and medialward (**13**). The genu internum n. facialis (**15**) is indicated just medial to the nucleus n. abducentis, the pars secunda of the radix n. facialis passing obliquely ventralward

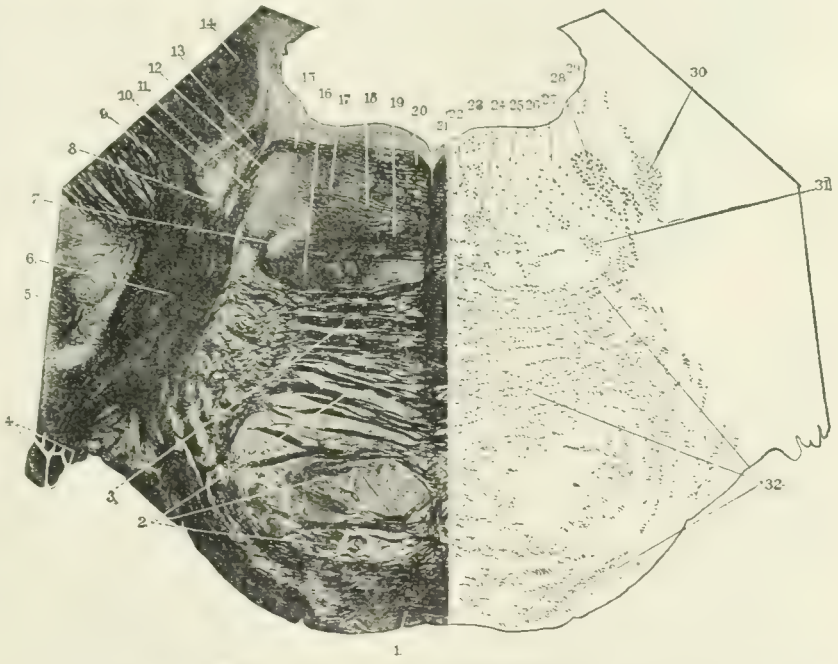

FIG. 916.—Transverse Section through the Pons at the Level of the Nervus Trigeminus in an Adult Human Being. On the left side the fibers have been photographed; on the right side the cell bodies have been drawn in. (After E. Flatau, "Atlas Cerebri Humani," Tab. xiii., Fig. A.) 1, Fibræ superficiales pontis; 2, fasciculi longitudinales pontis; 3, fibræ pontis profundæ; 4, radix nervi trigemini; 5, brachium pontis; 6, radix nervi trigemini; 7, nucleus olivaris superior; 8, radix nervi trigemini pars sensorius; 9, corpus restiforme; 10, nucleus sensorius nervi trigemini; 11, radix motorius nervi trigemini; 12, nucleus motorius princeps nervi trigemini; 13, radix descendens mesencephalica nervi trigemini; 14, brachium conjunctivum; 15, crossed fibers of nervus trigeminus; 16, lemniscus medialis; 17, formatio reticularis tegmenti; 18, fibræ arcuatæ internæ tegmenti; 19, fibræ arcuatæ internæ ventrales (compact bundle); 20, fasciculus longitudinalis medialis; 21, raphe; 22, cells of the middle line; 23, cells at the dorso-lateral part of the fasciculus longitudinalis medialis (connecting with the cells of the middle line); 24 and 25, nucleus centralis tegmenti, a large aggregation of cells in the tegmentum at the ventral part of the middle line (related to the nuclei pontis); 26, cells of the stratum griseum centrale; 27, scattered large cells of the tegmentum (nucleus magnocellularis diffusus of von Kölliker); 28, nucleus motorius princeps nervi trigemini; 29, cells of the locus cœruleus; 30 nucleus sensoruis nervi trigemini; 31, cells of the nucleus olivaris superior; 32, nuclei pontis.

contains the nuclei of the nerves connected with the pons, the fasciculus longitudinalis medialis, the medial and lateral lemnisci, the corpus trapezoideum, the formatio reticularis and the superior olivary complex. In Fig. 915 some of the principal structures of the lower part of the pons are shown. The section is taken at the level of the nuclei of origin of the n.

and lateralward at **11**. A portion of the nucleus n. vestibuli is shown near the floor of the fourth ventricle (**12, 20**), and lateral from it still some fibers of the radix descendens n. vestibuli (**10**). At this level the corpus restiforme (**9**) turns dorsalward to enter the cerebellum. The mass of fibers of the brachium pontis (**5**) are shown in their relation to the transverse fibers of the pons. Near the raphe, in the formatio reticularis, is a mass of cells, the so-called nucleus reticularis tegmenti of von Bechterew (**21**). The cells of the substantia gelatinosa (**22**) are seen chiefly medial to the fibers of the tractus spinalis n. trigemini (**8**).

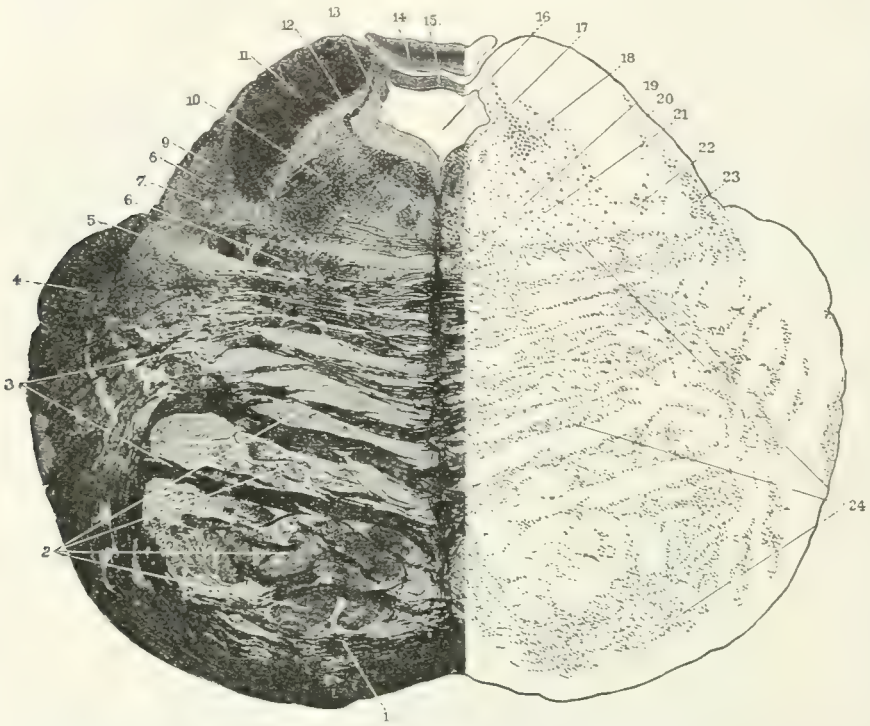

Fig. 917.—Transverse Section through the Pons in the Region of the Velum Medullare Anterius in an Adult Human Being. On the left side the fibers have been photographed; on the right side the cell bodies have been drawn in. (After E. Flatau, "Atlas Cerebri Humani," Tab. xiii., Fig. B.) 1, Fibræ pontis superficiales; 2, fasciculi longitudinales pontis; 3, fibræ pontis profundæ; 4, latero-dorsal compact peduncular part of pons; 5, latero-dorsal part of nuclei pontis; 6, lemniscus medialis; 7, nucleus lemnisci lateralis; 8, lemniscus lateralis; 9, continuation of nuclei pontis into lateral portion of tegmentum; 10, formatio reticularis tegmenti; 11, brachium conjunctivum; 12, radix descendens mesencephalica nervi trigemini; 13, fasciculus longitudinalis medialis; 14, lingula; 15, velum medullare anterius; 16, transition from the fossa rhomboidea to the aqueductus cerebri Sylvii; 17, aggregation of cells dorsal from the fasciculus longitudinalis medialis, continuous with the cells of the middle line; 18, cell bodies of the locus cœruleus; 19, continuation of the nuclei pontis into the tegmentum; 20, cells at the ventro-lateral periphery of the brachium conjunctivum; 21, scattered cells in the tegmentum (nucleus reticularis tegmenti of von Bechterew); 22, nucleus emnisci lateralis; 23, continuation of nuclei pontis into the lateral part of the tegmentum; 24, nuclei pontis.

Running transversely across the pons at the most ventral part of the pars dorsalis pontis are seen the fibers of the corpus trapezoideum, and in between these fibers run lengthwise the fibers of the lemniscus medialis (**3**). In the lateral part of the corpus trapezoideum is seen the nucleus olivaris superior (**6, 24, 25**). In the pars basilaris pontis are the fasciculi longitudinales (**2**), the fibræ pontis profundæ (**4**) and the fibræ pontis superficiales. In among these transverse and longitudinal bundles are situated the nuclei pontis (**27**). Some of the cells of this nucleus extend into the tegmental region (**26**).

A section through the pons at the level of the root of the n. trigeminus is illustrated in Fig. 916. Here the pars dorsalis pontis or tegmentum is more sharply differentiated from the pars basilaris pontis than in the previous section. The fourth ventricle is narrowing as the aqueduct of Sylvius is approached. The raphe (**21**) separates the two halves of the section from each other. Just lateral from the raphe on each side are seen the fibers of the fasciculus longitudinalis medialis. In the floor of the fourth ventricle are seen the cells of the stratum griseum centrale (**26**). At the lateral angle is a group of pigmented cells of the so-called locus cœruleus (**29**); the fibers of the corpus restiforme (**9**) are still visible at this level, and a cross-section of the fibers of the superior cerebellar peduncle or brachium conjunctivum (**14**) is met with. The junction of the n. trigeminus with the pons is shown at **4**, the radix n. trigemini at **6**. Lateral from it is seen the brachium pontis (**5**). The sensory portion of the root of the n. trigeminus (**8**) is distinguishable from the motor portion (**11**). The sensory nucleus of termination of the n. trigeminus (**10**) is situated more lateralward than the nucleus motorius princeps n. trigemini (**12**). The crossed fibers of the trigeminal root are indicated at **15**, while the radix descendens mesencephalica n. trigemini is shown at **13**. The fibræ arcuatæ internæ (**18**) are present in the tegmentum of the pons, but are not so much curved as those which were seen in the medulla oblongata. They are more compact in the ventral part of the tegmentum (**19**). The lemniscus medialis (**16**) is more laterally placed than in sections lower down. Just dorso-lateral from it is seen the nucleus olivaris superior (**7, 31**); the nucleus centralis tegmenti (**24, 25**) at this level makes a large mass of cells near the raphe on each side. In the pars basilaris pontis are seen the fasciculi longitudinales (**2**), fibræ pontis superficiales (**1**), the fibræ pontis profundæ (**3**), and the nuclei pontis (**32**).

A section taken at a higher level (Fig. 917) shows the beginning of the aqueductus cerebri (**16**), the roof of which is formed by the velum medullare anterius (**15**). Above this a cross-section of the lingula (**14**) is illustrated. In the lateral portion of the pars dorsalis pontis the large mass of fibers of the brachium conjunctivum (**11**) is seen. Lateral from the aqueductus cerebri are to be found the fibers of the radix descendens n. trigemini. In the floor of the aqueduct, close to the raphe on each side, is the fasciculus longitudinalis medialis (**13**); it is separated from the aqueduct by a mass of cells (**17**). The cells of the locus cœruleus (**18**) are situated just ventral from the radix descendens n. trigemini. The formatio reticularis tegmenti (**10**) contains scattered cells of the nucleus reticularis tegmenti (**21**). Ventro-lateral from the brachium conjunctivum are seen the fibers of the lemniscus lateralis, and among them the cells of the nucleus lemnisci lateralis (**22**). The

lemniscus medialis (**6**) forms a broad, flat ribbon in the floor of the pars dorsalis pontis. In the pars dorsalis pontis are met with again the fasciculi longitudinales (**2**), the fibræ pontis superficiales (**1**), the fibræ pontis profundæ (**3**), and the nuclei pontis (**24**).

The next section is taken at the level of decussation of the trochlear nerves of the two sides (Fig. 918). The lumen of the aqueductus cerebri (**20**) is small and diamond-shaped. In the roof is seen the decussatio nervorum trochlearium, and dorsal from it the lateral part of the velum medullare anterius (**16**). The radix n. trochlearis before decussation (**15**) is seen in the central gray matter (**21**). The locus cœruleus (**22**) here contains large cells. The comma-shaped cross-section of the fasciculus longitudinalis medialis (**18**) is a striking feature at this level. The lemniscus lateralis (**10**) is situated lateralward, many of its fibers coming into relation with the nucleus lemnisci lateralis (**11**). The lemniscus medialis (**7**) becomes displaced more and more lateralward. The brachium conjunctivum (**9, 12**) is undergoing decussation (**8**) at this level; its fibers run through the formatio reticularis tegmenti (**17, 25**). At the junction of the pars dorsalis with the pars basilaris pontis, near the middle line, is seen the tractus mamillo-peduncularis (Edinger), and lateral from it the bundle from the lemniscus medialis to the basis pedunculi. Close to the middle line, at about this level, are seen cells of the corpus interpedunculare (**28**). In the pars basilaris pontis the same structures are to be met with as at lower levels.

The next section (see Fig. 919) passes through the midbrain and shows the corpora quadrigemina and the pedunculi cerebri. In the middle line is situated the aqueductus cerebri (**24**). On each side of the aqueduct dorsalward the section passes through the superior colliculus of the corpora quadrigemina. The amount of the stratum griseum centrale (**25, 26**) is large in this region. In the superior colliculus passing from the dorsal surface inward can be seen the stratum zonale (**20**) or superficial white layer, the cappa cinerea (**17**) or superficial gray layer, the stratum opticum (**16**) or external grayish-white layer, the middle gray layer (**15**), the stratum lem-

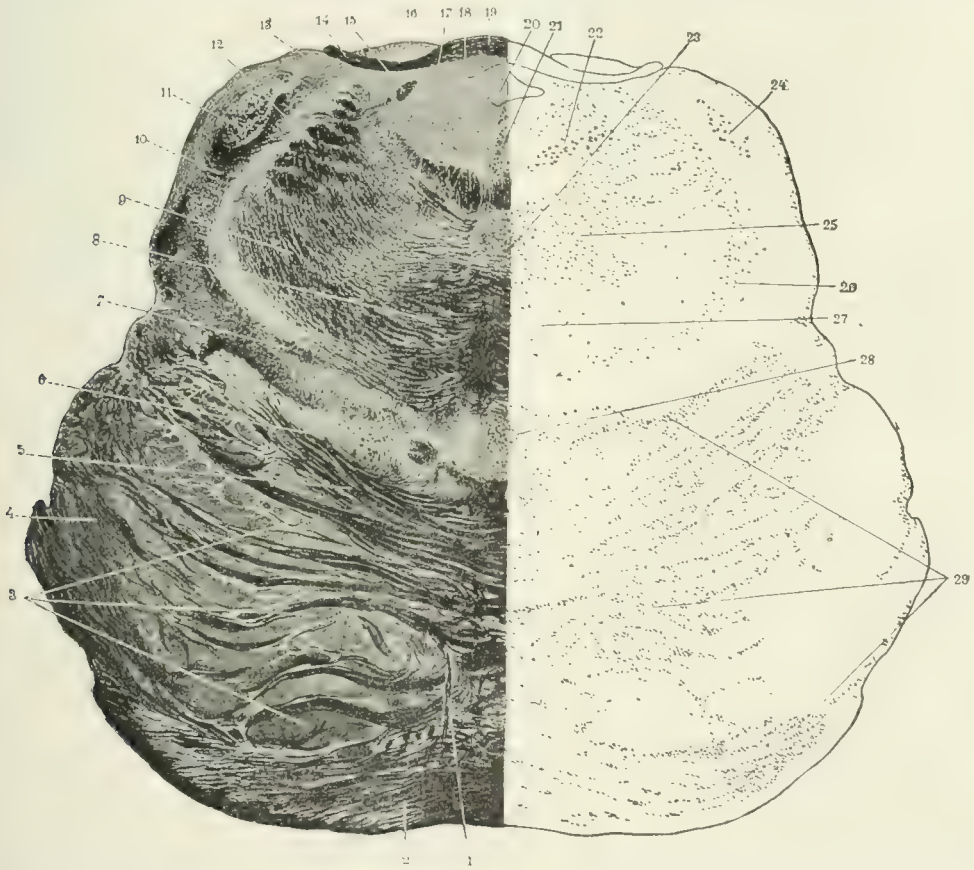

Fig. 918.—Transverse Section in the Region of the Proximal Portion of the Pons and of the Decussation of the Trochlear Nerves (Close Behind the Inferior Colliculi of the Corpora Quadrigemina) in an Adult Human Being. On the left side a photograph of the fibers is represented; on the right side the cell bodies have been drawn in from Nissl preparations. (After E. Flatau, "Atlas Cerebri Humani," Tab. xiv., Berlin, 1899.) 1, Blood-vessel; 2, fibræ pontis superficiales; 3, fasciculi longitudinales pontis; 4, lateral portion of basis pedunculi; 5, fibræ pontis profundæ; 6, tractus mamillo-peduncularis (Edinger) and lateral from it the bundle from the medial lemniscus to the pons (or to the basis pedunculi); 7, lemniscus medialis; 8, decussatio brachii conjunctivi; 9, brachium conjunctivum; 10, lemniscus lateralis; 11, bundles of the lateral lemniscus cut transversely (in the nucleus lemnisci lateralis); 12, brachium conjunctivum; 13, radial transverse bundles of the lemniscus lateralis passing across the radix descendens nervi trigemini; 14, nervus trochlearis after the decussation; 15, nervus trochlearis before the decussation; 16, lateral part of the velum medullare anterius going over into the substance of the tegmentum; 17, formatio reticularis tegmenti; 18, fasciculus longitudinalis medialis; 19, decussatio nervorum trochlearium; 20, aqueductus cerebri Sylvii; 21, cell bodies of the stratum griseum centrale; 22, cells of the locus cœruleus (the dorso-lateral cell bodies belong probably to the radix descendens nervi trigemini); 23, cell bodies of the middle line; 24, nucleus lemnisci lateralis; 25, cell bodies of the formatio reticularis; 26, gray intermediary layer of the formatio reticularis (dorso-medial from the lemniscus); 27, scattered cells in the neighborhood of the decussatio brachii conjunctivi; 28, cells of the corpus interpedunculare (substantia perforata posterior); 29, nuclei pontis.

nisci (**14**), the deep white layer (**19**), and the commissure between the two superior colliculi (**21**). The cerebral peduncle is divisible into two parts, the tegmentum and the basis pedunculi. Between the two is the substantia nigra (**3, 39**). In the tegmentum, below the stratum griseum centrale, are seen some deep arcuate fibers (**18**) which represent the continuation of the fibers of the deep white matter of the superior colliculus. The large nucleus ruber of the parts shown by the sections figured. The model was reconstructed from serial sections of the brain stem of a new-born babe, stained by the method of Weigert-Pal. Since at this age a considerable number of important fiber tracts (such, for instance, as the pyramidal tracts) are unmedullated, these are necessarily omitted from the model. This has the advantage, however, of bringing out the parts which are modeled in somewhat clearer relief, an advantage which is

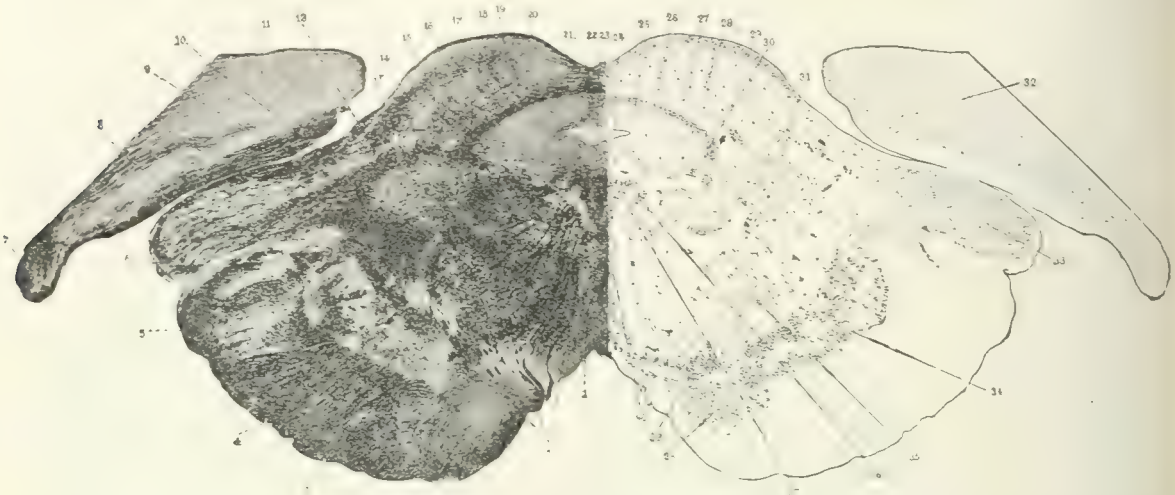

FIG. 919.—Transverse Section through the Superior Colliculi of the Corpora Quadrigemina and the Pedunculi Cerebri in an Adult Human Being. On the left side the fibers have been photographed; on the right the cells have been drawn in. (After E. Flatau, "Atlas Cerebri Humani," Berlin, 1899, Tab. xv.) 1, Ventral tegmental decussation of Forel; 2, radix nervi oculomotorii; 3, substantia nigra Soemmeringi; 4, basis pedunculi; 5, longitudinal bundles in the lateral part of the substantia nigra; 6, lemniscus medialis; 7, tractus opticus entering the corpus geniculatum laterale; 8, corpus geniculatum mediale; 9, formatio reticularis tegmenti; 10, brachium quadrigeminum superius; 11, thalamus; 12, lemniscus lateralis; 13, nucleus ruber (proximal part); 14, part of lemniscus medialis; 15, middle gray layer; 16, stratum opticum (external grayish-white layer); 17, cappa cinerea (superficial gray layer of superior colliculus); 18, deep arcuate fibers; 19, deep white layer of superior colliculus; 20, stratum zonale (superficial white layer of superior colliculus); 21, commissure of superior colliculi; 22, fasciculus longitudinalis medialis; 23, dorsal tegmental decussation of Meynert; 24, aqueductus cerebri Sylvii; 25, cell bodies in stratum griseum centrale; 26, aggregation of cells in peripheral part of stratum griseum centrale; 27, cell bodies of internal grayish-white layer; 28, cell bodies of middle gray layer with scattered large multipolar cells; 29, cell bodies of the cappa cinerea; 30, cell bodies of the radix descendens nervi trigemini; 31, aggregation of cell bodies in latero-dorsal part of tegmentum; 32, cells of distal part of thalamus (pulvinar); 33, cell bodies of corpus geniculatum mediale; 34, cell bodies of substantia nigra; 35, cell bodies of proximal part of nucleus ruber; 36, nucleus nervi oculomotorii extending ventralward into the region of the fasciculus longitudinalis medialis; 37, nucleus nervi oculomotorii; 38, most proximal remnant of nuclei pontis; 39, cell bodies of substantia nigra; 40, cell bodies of the middle line.

(**13**) is seen at this level in cross-section. The formatio reticularis (**9**) is very highly developed. Lateral from the nucleus ruber are seen the fibers of the lemniscus lateralis, and still more lateralward those of the brachium quadrigeminum superius (**10**). The corpus geniculatum mediale is shown at **8** and **33**, while the pulvinar of the thalamus is seen at **11** and **32**. Entering the corpus geniculatum laterale and the pulvinar is the tractus opticus (**7**). The fibers of the lemniscus medialis (**6**) are seen between the nucleus ruber and the substantia nigra. Near the middle line the fasciculus longitudinalis medialis (**22**) is met with in cross-section. Just dorsal to it is the nucleus n. oculomotorii (**36, 37**). The root fibers of this nerve (**2**) are shown passing ventralward to the interpeduncular space. The ventral tegmental decussation of Forel is visible at **1**.

The basis pedunculi consists of a compact mass of fibers that is sometimes known as the pes pedunculi cerebri. Through it run the fibers of the pyramidal tract, those of the frontal cerebrocorticopontal path, and those of the temporal cerebrocorticopontal path.

The Brain Stem, Models.—A synthetic picture in three dimensions of the structures shown in these cross-sections is given by the wax models constructed by Dr. Florence R. Sabin (1901). The accompanying illustrations (Figs. 920, 921, 922, 923, and Plate XVI) will permit the reader to see the complete form of most of especial significance since the tracts fully medullated at birth are in general those concerned with the more fundamental reflex systems.

As seen from the dorsal surface (Fig. 920), the boundaries of the fourth ventricle give an important guide to the position of the underlying parts (cf. Fig. 905). Running through the entire length of the model near the mid-line is the fasciculus longitudinalis medialis (Figs. 920, **12**; 922, **19**; 923, **27**). This is an association tract related chiefly with the somatic motor centers, extending forward as far as the thalamus and backward into the fasciculus proprius ventralis of the spinal cord. At the lower end of the model the ascending fibers of the medial lemniscus are seen leaving the nuclei of the funiculus gracilis and cuneatus, soon to cross in the decussation of the lemniscus (Fig. 923, **11**) and then to ascend ventrally of the fasciculus longitudinalis medialis. From the funiculus lateralis of the spinal cord fibers ascend (Fig. 921, **33**) to join the lemniscus in the neighborhood of the pons. These constitute the spinal component of the lemniscus. At the level of the VIII. nuclei the lateral lemniscus receives a great addition from these nuclei and from the superior olive, chiefly by way of the corpus trapezoideum (Figs. 923, **6, 7**; 922, **34**). Most of the fibers of the lateral lemniscus enter the colliculus inferior (Figs. 920, **34**; 921, **39**; 922, **8**; 923, **28**), while the medial lemniscus and most of the spinal component of the lemniscus ascend to the thalamus

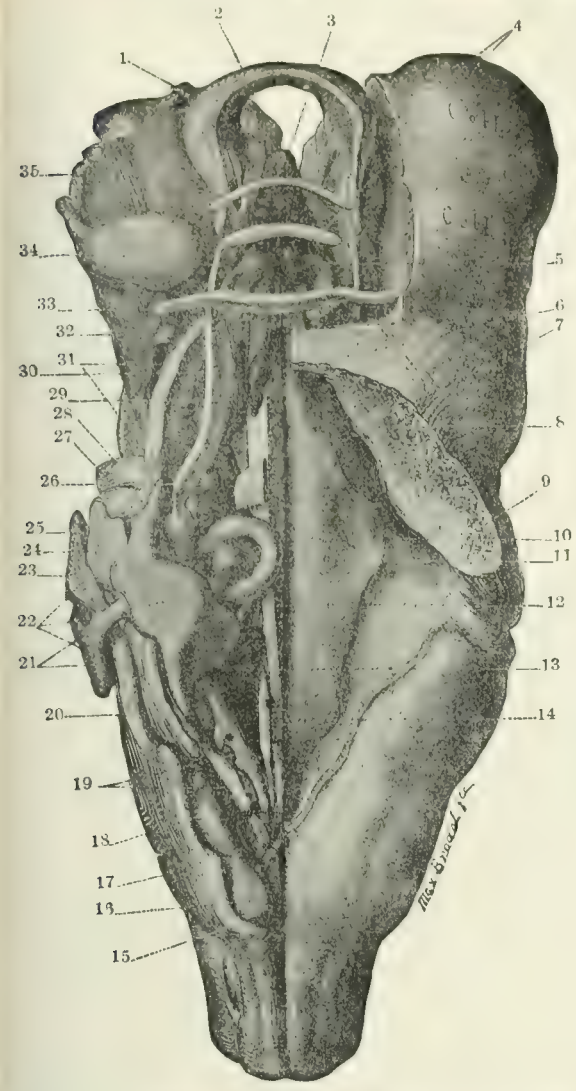

Fig. 920.—View of the Sabin Model from the Dorsal Surface. The right side of the view shows the surface form, the left structures of the model. The position of these structures can be related to the dorsal funiculi of the spinal cord, the fourth ventricle, and the inferior and superior colliculi. 1, Fasciculus retroflexus (Meynerti); 2, stratum album profundum; 3, nucleus n. oculomotorii; 4, commissuræ nuclei colliculi inferioris; 5, nucleus n. trochlearis; 6, substantia ferruginea; 7, ventriculus quartus; 8, brachium conjunctivum; 9, corpus restiforme; 10, radix n. facialis (genu internum); 11, nucleus n. abducentis; 12, fasciculus longitudinalis medialis; 13, nucleus olivaris inferior; 14, nucleus n. hypoglossi; 15, fasciculus gracilis; 16, nucleus funiculi gracilis; 17, fasciculus cuneatus; 18, nuclei funiculi cuneati; 19, tractus solitarius et nucleus alæ cinereæ; 20, corpus restiforme; 21, nucleus n. cochleæ dorsalis; 22, nucleus et radix n. vestibuli; 23, corpus restiforme; 24, nucleus n. vestibuli lateralis; 25, nucleus n. trigemini (sens.); 26, nucleus motorius princeps n. trigemini; 27, radix n. trigemini (sens.); 28, radix n. trigemini (mot.); 29, locus cœruleus; 30, radix descendens n. trigemini; 31, brachium conjunctivum; 32, same as 8, Fig. 921; 33, radix n. trochlearis; 34, nucleus colliculi inferioris; 35, lemniscus medialis.

Nucleus et radix n. vestibuli: The ascending root is marked by the most proximal of the three lines on the figure; the descending by the most distal line, while the nucleus n. vestibuli medialis is indicated by the middle of the three lines. The nucleus n. vestibuli superior is continuous with the medial nucleus and lies oppsite the ascending root. The nucleus n. vestibuli lateralis consists of two parts, one between the corpus restiforme and the ascending root, the other in the notch between the medial and superior nuclei.

Nucleus n. cochleæ dorsalis: The more proximal of the two lines points to the striæ acusticæ. (After Sabin.)

(Figs. 920, **35**; 922, **42**). Around the axis formed by these great longitudinal conduction systems the cerebral nerves, their nuclei and association tracts, the cerebellar connections, etc., are laid down as illustrated in the figures. The form of the inferior olive is illustrated in Fig. 924. Its chief connections are shown diagrammatically in Fig. 932.

We shall next review the chief features of the central connections of the several cerebral nerves.

The oculomotor nerve is known to contain three components: (1) somatic motor fibers for the innervation of the muscles of the orbit, viz., the musculi levator palpebræ, obliquus inferior, rectus superior, rectus internus and rectus inferior; (2) visceral motor fibers for the ciliary ganglion; (3) fibers of deep sensibility for the orbital muscles above mentioned. The motor nuclei lie in the floor of the aqueduct of Sylvius (Fig. 919, **36, 37**) and are three in number, the lateral, medial and small-celled nucleus. The large multipolar cells of the lateral and medial nuclei supply the somatic motor fibers of the third nerve and are arranged as shown in the diagrams (Figs. 925, 950). The small-celled nucleus, or nucleus of Edinger-Westphal (Fig. 925, *a*, *b*) is supposed to supply the visceral motor fibers for the ciliary ganglion, chiefly serving as constrictors of the iris. Edinger (1911, p. 310) considers it probable that the tractus peduncularis transversus and its ganglion lying between the pes pedunculi and the corpus mammillare are parts of this visceral motor system and that it also receives fibers directly from the optic tract for optic reflexes of accommodation. Sherrington and Tozer (*Proc. Roy. Soc.*, 1910) have shown that the III., IV., and VI. nerves carry afferent fibers of muscle and tendon sensibility, which enter the cranial cavity in company with motor root fibers. Their central connections are unknown.

The trochlear nerve contains somatic motor and somatic sensory (proprioceptive) fibers. The former arise from a nucleus lying immediately caudad of the lateral nucleus of the III. nerve and supply the superior oblique muscle of the eyeball. The afferent fibers supply deep sensibility to the same muscle. This nerve turns dorsally and backward to decussate in the velum medullare anterius before it leaves the brain (Fig. 918, **14, 15**). No satisfactory explanation of this aberrant course of the IV. nerve has been suggested.

The abducens nerve supplies with its somatic motor fibers the external rectus muscle of the eyeball and it contains afferent fibers from the same muscle. Its nucleus lies close under the floor of the fourth ventricle and is embraced by the genu of the facial nerve (Fig. 915, **14, 18**). A smaller ventral nucleus of the VI. nerve, near the chief motor VII. nucleus has also been described by several authors.

The three eye-muscle nerves are intimately connected with the optic centers in the roof of the colliculus superior by way of the fibers of the posterior commissure and the fasciculus longitudinalis medialis. The latter bundle also carries ascending fibers from the nucleus lateralis vestibuli (Deiters). These connections provide pathways for the nervous impulses necessary respectively for the fixation of objects in the field of vision and for the reflex coordination of stimuli from the labyrinth and the eyes in equilibration and bodily orientation. The coordination of movement of the six muscles of the two eyeballs with each other and with the other bodily muscles is effected chiefly by ascending and descending fibers between the nuclei of the III., IV. and VI. nerves and other somatic motor centers in the fasciculus longitudinalis medialis. There is also a direct tract from the nucleus olivaris superior to the nucleus nervi abducentis (Fig. 930), thus putting the primary acoustic center into immediate reflex connection with the external rectus muscle of the eye of the same side. The cortical path of the eye-muscle nuclei has not been accurately determined, but fibers are seen to pass dorsally through the tegmentum from

the pyramidal tracts to the vicinity of these nuclei, which probably serve this function.

The trigeminus nerve has two roots, known respectively as the portio major and the portio minor. The former is exclusively sensory, its fibers belonging to the somatic sensory group. Its ganglion is the semilunar or Gasserian ganglion, and its fibers supply general sensibility to the skin of most of the head, to the greater part of the mucous lining of the mouth cavity, and to the anterior two-thirds of the tongue. Centrally these fibers in part terminate in the so-called chief sensory nucleus at the level of entrance of the root (Fig. 916, 10) and in part turn abruptly backward toward the spinal cord to form the tractus spinalis nervi trigemini and to terminate in the spinal nucleus of the V. nerve which accompanies this tract for its entire length and is known as the substantia gelatinosa of Rolando (Figs. 907 to 915). The spinal V. tract extends into the spinal cord as far as the second cervical nerve. Some collaterals of these fibers pass through the substantia gelatinosa to terminate in the motor nuclei of the V., VII. and XII. nerves. Some root fibers of the trigeminus also extend medialward and backward to enter the rostral end of the fasciculus solitarius.

The cerebral pathways for fibers of the second order connected with this root in part pass to the motor nuclei of the oblongata and to the tegmentum for simple reflexes and in part enter the lemniscus system for the higher cerebral centers. Of the latter, there are two chief pathways. (1) The dorsal secondary trigeminal path arises chiefly from the spinal nucleus and ascends in the dorsolateral part of the tegmentum to reach the rostral end of the lateral or ventral nucleus of the thalamus. This is partly an uncrossed tract, but there are also crossed fibers which lie somewhat farther ventral than the others. Many of its fibers terminate in the tegmentum before reaching the thalamus. (2) The ventral sceondary trigeminal path arises chiefly from the frontal pole of the chief sensory nucleus, decussates in the ventral tegmental decussation, turns forward in a position dorsomedially of the medial lemniscus and terminates chiefly in the rostral end of the ventral nucleus of the thalamus and also in the centre médian of Luys (nucleus medialis b, of von Monakow, Fig. 945). The ventral path has been demonstrated by Wallenberg in birds as passing from the sensory trigeminus nucleus directly forward through the midbrain and thalamus, to which it contributes

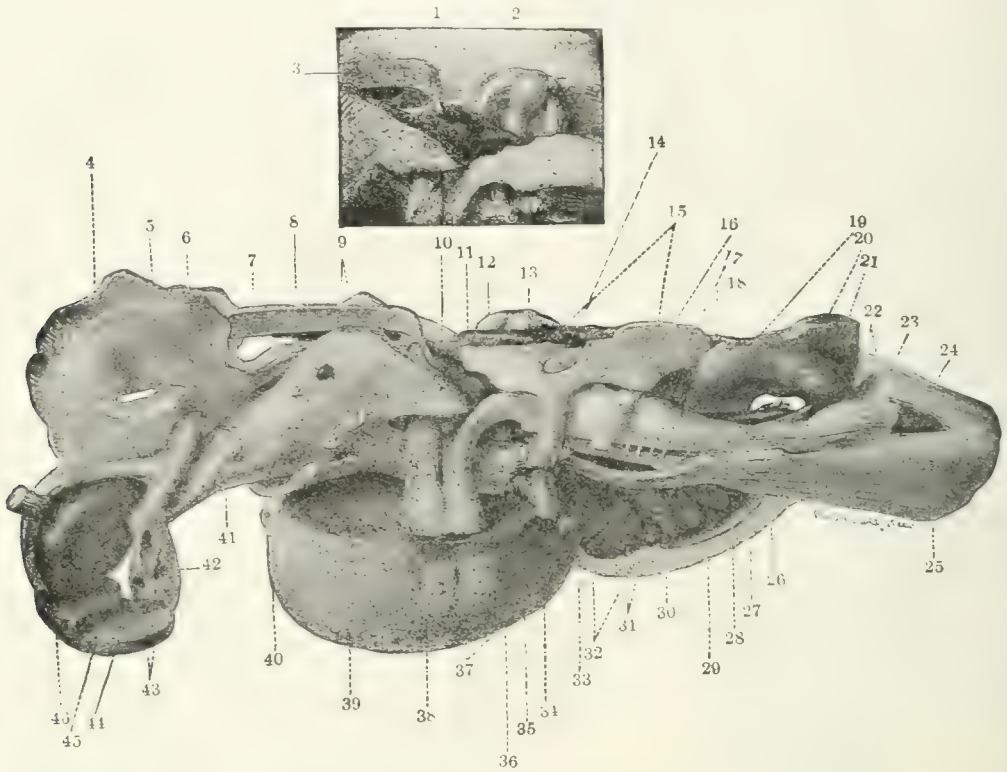

Fig. 921.—View of the Model from the Lateral Aspect, after the Removal of the Following Structures: The Corpus Restiforme, the Substantia nigra, and the Medial, Lateral, and Superior Lemnisci. The view is designed to show (1) the sensory nerves and their nuclei, and (2) the midbrain. The nuclei of the dorsal funiculi represent a way station for the sensory fibers from the spinal cord; the sensory cerebral nerves are represented by the nuclei nervi glosso-pharyngei, vagi, vestibuli, et trigemini. These include all of the sensory nerves of the region of the model, except the n. cochleæ, which was removed with the corpus restiforme. 1, Nucleus motorius princeps n. trigemini; 2, nucleus n. trigemini (sensory); 3, radix descendens n. trigemini; 4, stratum album profundum; 5, nucleus n. oculomotorii; 6, radix n. oculomotorii; 7, radix descendens n. trigemini; 8, fibers running from lemniscus lateralis to the brachium conjunctivum; 9, brachium conjunctivum; 10, fasciculus longitudinalis medialis; 11, nucleus n. vestibuli superior; 12, radix n. facialis (genu internum); 13, nucleus n. abducentis; 14, nucleus n. vestibuli lateralis; 15, radix descendens et ascendens n. vestibuli; 16, fibers to tractus solitarius; 17, radices n. IX. and X.; 18, tractus solitarius; 19, nucleus funiculi cuneati; 20, nucleus funiculi gracilis; 21, nucleus funiculi cuneati lateralis; 22, fasciculi graciles; 23, fasciculus cuneatus; 24, substantia gelatinosa (Rolandi); 25, fasciculus cerebello-spinalis; 26, fibræ arcuatæ internæ (distal bundle); 27, substantia gelatinosa (Rolandi); 28, fasciculus cerebello-spinalis; 29, radix n. hypoglossi; 30, nucleus olivaris inferior; 31, radices n. IX. and X.; 32, tract from Deiters' nucleus to spinal cord; 33, fasciculus lateralis; 34, radix n. vestibuli; 35, radix n. facialis; 36, corpus trapezoideum; 37, radix n. trigemini (sens.); 38, radix n. trigemini (mot.); 39, lemniscus lateralis; 40, lemniscus medialis; 41, fibers to decussatio tegmenti dorsalis; 42, radix n. oculomotorii; 43, nucleus columnaris; 44, nucleus capsulæ lateralis nuclei rubri; 45, lectus substantiæ nigræ; 46, nucleus ruber.

Radix n. trigemini (sens.): The proximal line runs to the root bundle, the distal to the tractus spinalis n. trigemini. (After Sabin.)

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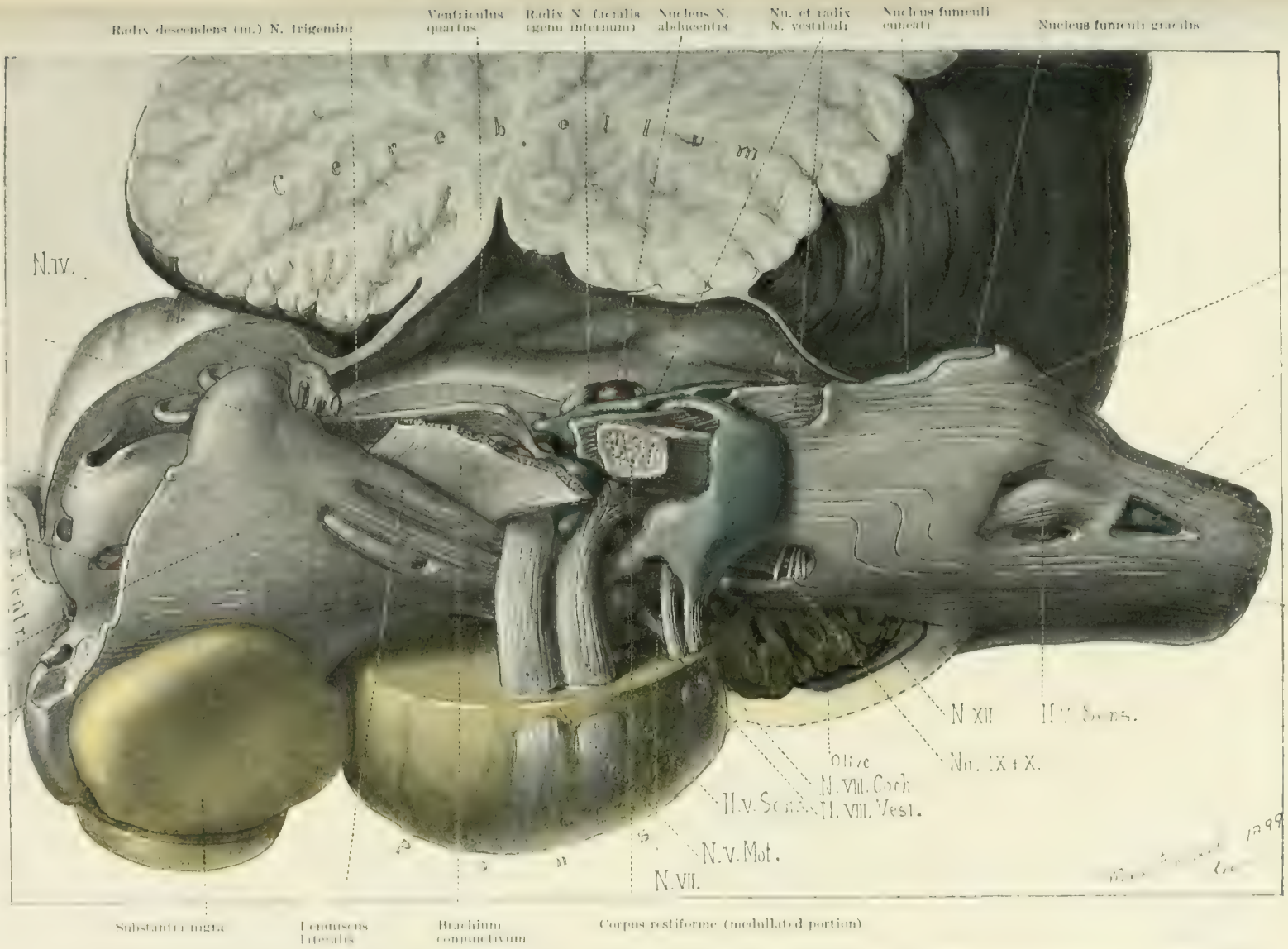

A WAX PLATE RECONSTRUCTION OF THE MEDULLA, PONS, AND MIDBRAIN OF THE NEWBORN BABE. MOTOR NUCLEI RED; SENSORY NUCLEI BLUE, OTHER NUCLEI YELLOW
(After Florence R. Sabin, Welch Volume of Contributions to Medical Science, 1900.)

some fibers, and a part of its fibers continue still farther forward without interruption through the cerebral hemisphere to end in the area parolfactoria, or tuberculum olfactorium. This tract he terms the tractus quintofrontalis. No fibers of the trigeminal lemniscus are known to extend farther forward than the thalamus in mammals.

Direct root fibers have been described from the trigeminus to the cerebellum. These apparently do not occur in mammals, though fibers of the second order undoubtedly connect with the cerebellum.

The portio minor of the trigeminus root (nervus masticatorius) is of mixed function. The greater part is motor for the innervation of the muscles of mastication. These fibers arise from the chief motor V. nucleus (nucleus masticatorius) at the level of the superficial origin of the root (Fig. 63, **12**). The cortical lated, are the processes of the large vesicular cells of the mesencephalic nucleus of the trigeminus which form a slender gray column accompanying the root fibers (Fig. 919, **30**).

Between the chief motor nucleus and the mesencephalic nucleus is a considerable collection of cells, the locus coeruleus (Fig. 917, **18**), which is commonly regarded as a part of the motor V. nucleus. Its connections and functions are, however, still very uncertain. Scattered among its characteristic polymorphic and pigmented cells are others of the same form as those of the mesencephalic nucleus and probably of the same type.

The mesencephalic V. nucleus is regarded by Johnston and others as composed of cells of the same type as those of the spinal ganglia, which were incorporated into the neural tube from the neural crest in early em-

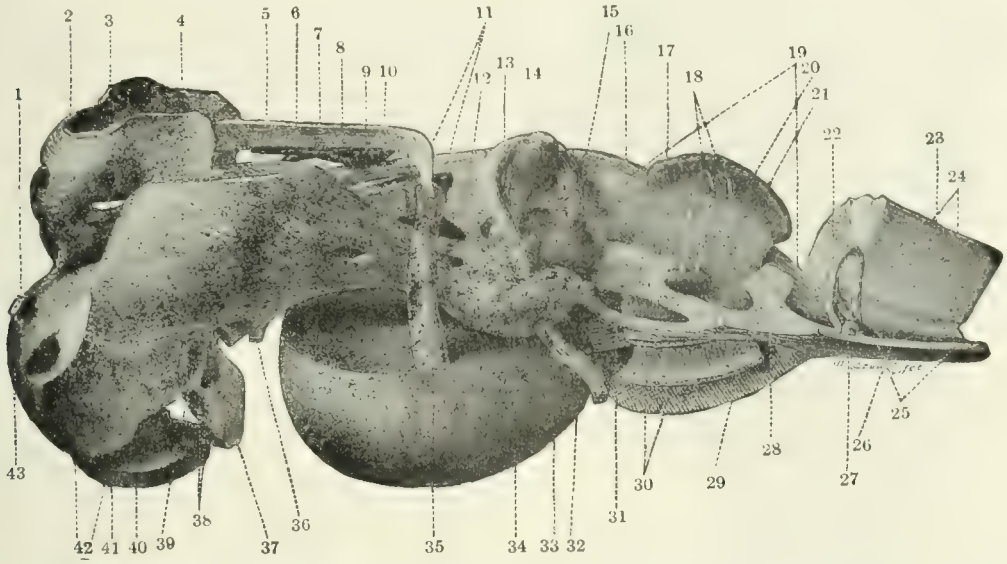

Fig. 922.—View of the Model from the Lateral Aspect. The sensory nerves of Fig. 921 have been removed and all of the motor cerebral nerves except the n. trochlearis are now shown. 1, Fasciculus retroflexus (Meynerti); 2, capsula dorsalis nuclei rubri; 3, nucleus n. oculomotorii; 5, radix descendens n. trigemini; 6, lemniscus medialis; 7, locus cœruleus; 8, lemniscus lateralis; 9, fasciculus longitudinalis medialis; 10, formatio reticularis alba; 11, nucleus motorius princeps n. trigemini; 12, formatio reticularis alba; 13, radix n. facialis (genu internum); 14, nucleus n. abducentis; 15, nucleus n. facialis; 16, tract from Deiters' nucleus to funiculus lateralis; 17, nucleus ambiguus; 18, radices n. IX. and X. (mot.); 19, fasciculus longitudinalis medialis; 20, nucleus n. hypoglossi; 21, radix n. hypoglossi; 22, radix n. accessorii; 23, fasciculus gracilis; 24, canalis centralis; 25, position of columna ventralis; 26, fasciculus ventralis proprius; 27, fasciculus cerebello-spinalis; 28, fasciculus cerebello-spinalis; 29, fasciculus lateralis; 30, radix n. hypoglossi; 31, nucleus olivaris accessorius medialis; 32, nucleus olivaris superior; 33, radix n. facialis, pars secunda; 34, corpus trapezoideum; 35, radix n. trigemini (mot.); 36, lemniscus medialis to substantia nigra; 37, radix n. oculomotorii; 38, nucleus columnaris; 39, nucleus capsulæ lateralis nuclei rubri; 40, lectus substantiæ nigræ; 41, capsula lateralis nuclei rubri; 42, lemniscus medialis; 43, capsula superior nuclei rubri. (After Sabin, F. R.)

center for the motor V. nucleus lies in the lower third of the precentral gyrus and perhaps in neighboring parts of the middle and inferior frontal gyri. Its projection fibers descend through the genu of the internal capsule and accompany for some distance the medial lemniscus, then decussate under the inferior colliculus before effecting connection with the motor V. nucleus.

The mesencephalic (cerebral or descending) root of the trigeminus is commonly described as motor, though the particular muscles innervated are not stated. Recent experimental work has shown that this root is probably sensory in function, supplying muscular sensibility to several muscles of the head (not including the eye muscles). Its fibers turn forward along the lateral border of the aqueduct of Sylvius (Figs. 916, **13**; 917, **12**) for the entire length of the midbrain. These fibers, which are heavily medullbryonic stages. Ramón y Cajal has shown that the fibers of the mesencephalic root give off large numbers of fine collaterals which terminate around the bodies of the cells of the chief motor V. nucleus. These probably represent pathways of direct reflex connection from the sense organs within the muscles of mastication to the motor centers from which these muscles are innervated, though Ramón y Cajal himself suggests a different interpretation. He regards the mesencephalic root as motor and is of the opinion that by means of the collateral connection of its fibers with the chief motor nucleus a relatively weak stimulus from the mesencephalic nucleus may be reinforced in the chief nucleus, thus providing a much more powerful and sustained contraction of the jaw muscles than the mesencaphalic nucleus alone would be able to do. A very complete experimental study of the mesencephalic

root has been made by Willems (Le Névraxe, vol. xii., 1911), who cut the different motor branches of the V. nerve in the rabbit and determined by study of the resultant chromatolysis the number and localization in the chief motor nucleus of all of the cells which innervate the several trigeminal muscles. After cutting these

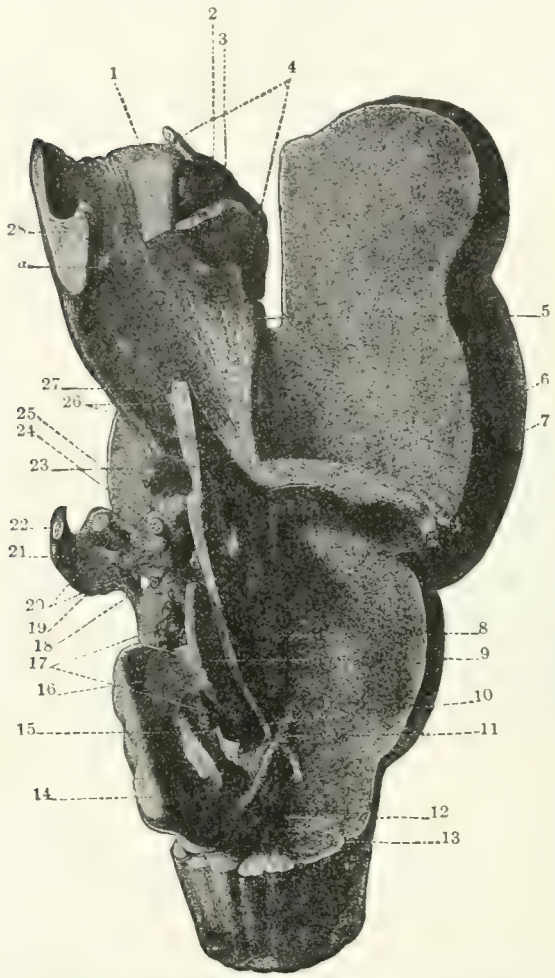

FIG. 923.—View of the Model from a Dorso-median Aspect. This view is designed to show the central fiber mass, that is, the medulla, pontal and midbrain sheets, together with the corpus trapezoideum. 1, Capsula superior nuclei rubri; 2, radix n. oculomotorii; 3, nucleus ruber; 4, fasciculus retroflexus (Meynerti); 5, lemniscus medialis; 6, corpus trapezoideum; 7, nucleus olivaris superior; 8, stratum interolivare lemnisci; 9, nucleus n. hypoglossi; 10, nucleus olivaris accessorius medialis; 11, decussatio lemniscorum; 12, canalis centralis; 13, substantia gelatinosa (Rolandi); 14, nucleus funiculi gracilis; 15, fasciculus cuneatus to formatio reticularis; 16, nucleus funiculi cuneati; 17, nucleus olivaris inferior; 18, radix n. cochleæ; 19, corpus trapezoideum; 20, radix n. vestibuli; 21, nucleus n. cochleæ dorsalis; 22, striæ acusticæ; 23, nucleus n. abducentis; 24, radix n. facialis; 25, nucleus olivaris superior; 26, formatio reticularis alba; 27, fasciculus longitudinalis medialis; 28, lemniscus lateralis.

α, Fibers running from lemniscus lateralis to the brachium conjunctivum. (After Sabin.)

motor branches, the mesencephalic nucleus also shows chromatolysis, but at a different rate from that of the chief nucleus. Since all of the muscular branches were shown to be represented in the chief motor nucleus, he assumes that the mesencephalic nucleus supplies sensory fibers to the muscles.

The chief connections of the nervus trigeminus are indicated diagrammatically on Fig. 926.

The facial nerve has two roots, the portio dura which is exclusively motor, and the portio intermedia, or nerve of Wrisberg. The fibers of the portio dura arise from a compact nucleus of large cells belonging to the ventrolateral series (Figs. 905 and 914, **32**). Functionally they belong to the specialized visceral motor system and supply the facial musculature exclusive of the muscles of mastication, all of these muscles being embryologically derived from the branchial muscles of the hyoid segment. These root fibers pass dorsalward and medialward and close under the floor of the fourth ventricle they turn lateralward around the nucleus of the VI. nerve. The genu of the facial nerve which is thus formed, together with the VI. nucleus, produce an eminence in the floor of the ventricle which is variously named the eminentia teres, eminentia facialis and eminentia abducentis.

The cortical center for the motor facialis root lies in the lower part of the precentral convolution and its projection fibers descend through the genu of the internal capsule and the medial part of the pyramidal tract. (See Fig. 934, *tr. cort.-bulb.m.*) These fibers leave the pyramidal tract near the transverse plane of the motor VII. nucleus and cross the raphe to reach it. Root fibers of the V. nerve reach the motor VII. nucleus for facial reflexes; the other cerebral nerves are also connected with it through the reticular formation.

The portio intermedia of Wrisberg is a mixed facial root, containing visceral afferent and visceral efferent fibers. The afferent fibers arise from cells of the geniculate ganglion and are of two sorts: (1) unspecialized fibers of sympathetic type, and (2) specialized visceral sensory fibers serving the sense of taste in the anterior two-thirds of the tongue and reaching the brain by way of the chorda tympani. Both sorts of afferent fibers enter the fasciculus solitarius and end in the nucleus which accompanies this fasciculus. This nucleus effects secondary connections with the chief motor nuclei of the V., VII., IX., X., and XII. nerves for the gustatory reflexes of mastication, etc. The course of the secondary path from this nucleus to the cerebral hemisphere is wholly unknown in mammals.

The efferent fibers of the portio intermedia belong to the unspecialized visceral efferent type and are chiefly concerned with salivary secretion. There are two salivatory nuclei, the superior connected with the facial nerve and the inferior connected with the glossopharyngeal nerve. The nucleus salivatorius superior lies dorsolaterally of the chief motor VII. nucleus (between the points marked **22** and **23** in Fig. 915) and innervates the submaxillary and some other glands by way of the chorda tympani nerve.

The relations of the roots of the facialis nerve are shown on Fig. 927, the portio dura on the left and the portio intermedia on the right.

The acoustic nerve has two roots, the radix cochlearis (lateral, ventral, posterior or superficial root) devoted to the sense of hearing, and the radix vestibularis (medial, dorsal, anterior or deep root) devoted chiefly to equilibratory reactions, the proprioceptive reflexes of Sherrington. The primary center into which these fibers discharge is widely diffused; taken as a whole it is known as the area acustica. The vestibular root is the more primitive, it alone being present in the lower vertebrates. In the embryo the VIII. nuclei are developed from the rhomboidal lip in the region of the facial nerve and represent a differentiation of the somatic sensory column, whose unspecialized component is reduced in this region. In the course of development the vestibular nuclei spread out medialward over the floor of the fourth ventricle and the cochlear nuclei spread out lateralward around the corpus restiforme to form the dorsal cochlear nucleus, or tuberculum acusticum, and the ventral cochlear nucleus (Fig. 914), the latter ex-

tending even beyond the limits of the brain outward into the cochlear root. The vestibular nuclei, together with fibers of the cochlear system which cross the floor of the fourth ventricle (striæ medullares acusticæ), spread medialward and more or less obliterate the sulcus limitans, vestiges of which are preserved both above and below this level (Figs. 903, 905).

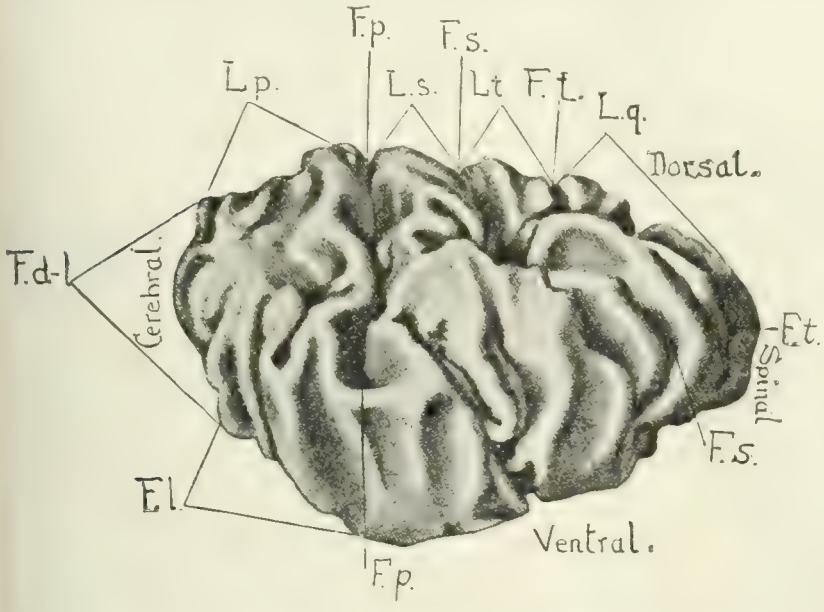

Fig. 924.—View of the Dorso-lateral and Lateral Surfaces of the Nucleus Olivaris Inferior. *f.dl.*, Facies dorso-lateralis; *f.l.*, facies lateralis; *f.p.*, fissura prima; *f.s.*, fissura secunda; *f.t.*, fissura tertia; *l.p.*, lobus primus; *l.s.*, lobus secundus; *l.t.*, lobus tertius; *l.q.*, lobus quartus.

The vestibular (equilibratory) and cochlear (auditory) fibers are more or less mingled in the VIII. nerve and their cerebral centers are likewise incompletely separated. In general, the cochlear fibers terminate in or pass through the ventral or dorsal cochlear nucleus on the lateral surface of the medulla oblongata, while the vestibular fibers terminate in or traverse the vestibular nuclei farther medially. The topographic relations of these nuclei to one another and to the surrounding structures in the oblongata of the new-born babe are shown in flat projection upon the horizontal plane in the accompanying figure (Fig. 928) after Miss Sabin, and the relations of most of these nuclei are seen in transverse section in Fig. 914. See also Figs. 920, 929, 930.

The radix vestibularis passes into the oblongata medially of the corpus restiforme. Its fibers bifurcate into ascending and descending branches, of which the latter for the most part enter the spinal vestibular nucleus. There are four vestibular nuclei: (1) the nucleus nervi vestibuli superior (nuc. angularis, nuc. of Bechterew or Flechsig, *S* on Figs. 928 and 929); (2) the nucleus nervi vestibuli lateralis (nuc. vestibuli magnocellularis, nuc. of Deiters, *L*, *L*[1]); (3) the nucleus nervi vestibularis medialis (nuc. dorsalis, nuc. triangularis, nuc. of Schwalbe, *M*, *Y*); (4) the nucleus nervi vestibularis spinalis (receiving the radix descendens, Fig. 928, *R.d.n.ve.*, Fig. 929, *Sp.*).

Root fibers of the vestibular nerve reach all of these nuclei and some also pass directly upward into the cerebellum in company with the secondary fibers of the tractus vestibulo-cerebellaris. The latter tract is made up chiefly of axones of cells of the superior and lateral vestibular nuclei, with some from the medial nucleus. There is also a descending tract from the cerebellum to the vestibular nuclei. The ascending fibers decussate for the most part in the cerebellar commissure and terminate chiefly in the roof nuclei of the opposite side of the vermis; also in the nucleus dentatus. These pathways play a very important part in the proprioceptive functions of bodily equilibration and the maintenance of muscular tone. The superior nucleus (and according to some authors the lateral nucleus also) sends a strong secondary tract into the fasciculus longitudinalis medialis of both sides for motor coordination. The most important of these connections is with the nuclei of the eye muscles. The medial nucleus sends fibers to the reticular formation of the same and the opposite side for connection with the motor centers of the oblongata. The lateral and spinal nuclei contribute secondary

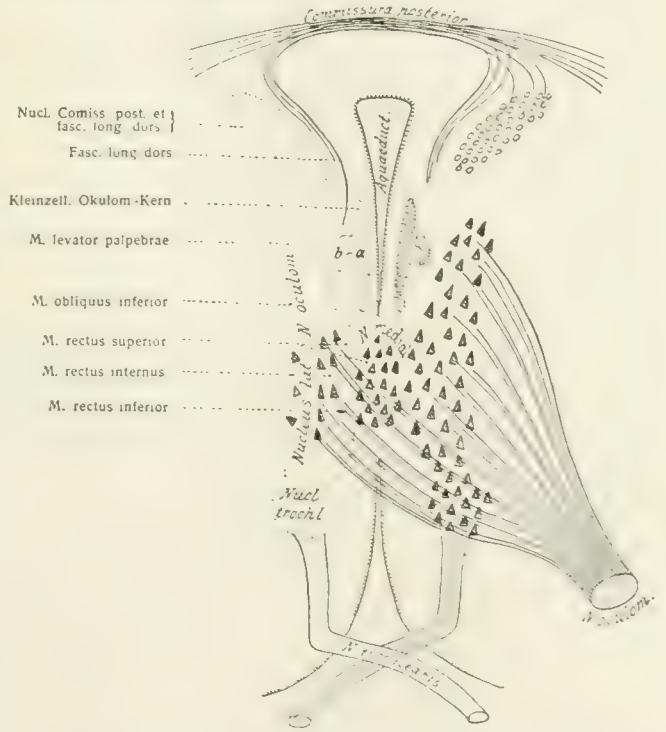

Fig. 925.—Diagram of the Motor Nuclei of the III. and IV. Cerebral Nerves as seen from Above. The localization of the oculomotorius nuclei in part after the researches of Bernheimer on apes. *a*, *b*, The small-celled nucleus, or nucleus of Edinger-Westphal, probably visceral motor in function and connected with the ciliary ganglion. The other nuclei shown are somatic motor in function. (After Edinger.)

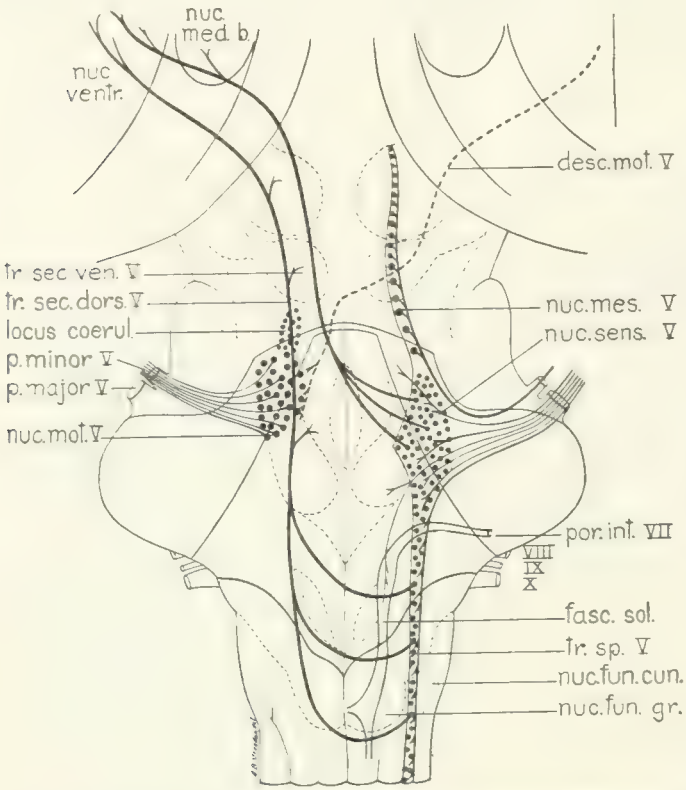

FIG. 926.—Diagram of the Nuclei of the V. Cerebral Nerve, together with Some of the Secondary Connections. The motor root is drawn on the left side and the sensory roots on the right; cf. Fig. 905. *desc. mot. V.*, Descending tract from cerebral cortex to the motor V. nucleus; *fasc. sol.*, fasciculus solitarius; *locus cærul.*, locus cœruleus; *nuc. fun. cun.*, nucleus funiculi cuneati; *nuc. fun. gr.*, nucleus funiculi gracilis; *nuc. med. b.*, nucleus medialis b (of von Monakow, centre médian of Luys) of the thalamus; *nuc. mes. V.*, nucleus mesencephalicus trigemini; *nuc mot. V.*, nucleus motorius princeps trigemini; *nuc. sens. V.*, nucleus sensitivus princeps trigemini; *nuc. sp. V.*, nucleus spinalis trigemini; *nuc. ventr.*, nucleus ventralis thalami; *p. major V.*, portio major trigemini; *p. minor V.*, portio minor trigemini; *por. int. VII.*, portio intermedia (Wrisbergi) facialis; *tr. sec. dors. V.*, dorsal secondary trigeminus tract; *tr. sec. ven. V.*, ventral secondary trigeminus tract; *tr. sp. V.*, tractus spinalis trigemini.

fibers to a vestibulospinal tract which descends without decussation into the ventrolateral funiculus of the spinal cord.

Some fibers from the vestibular nuclei are said to pass through the striæ medullares acusticæ to the lemniscus of the opposite side and thence to the inferior colliculus. But the number of such fibers is small and their presence is controverted. The cortical connections of the vestibular nerve are relatively unimportant, for its functions belong to the proprioceptive system of reflexes and involve small conscious control.

The radix cochlearis discharges chiefly into the two cochlear nuclei, though probably many root fibers pass through these nuclei and accompany the secondary tracts. The dorsal nucleus (lateral nucleus or tuberculum acusticum), lies dorsally and laterally of the corpus restiforme (Fig. 914, **14**); the ventral nucleus, or nucleus accessorius (Fig. 914, **12**), lies ventrally of the corpus restiforme and extends outward for some distance into the cochlear root. The structure of these nuclei and of their secondary connections is very complex. The root fibers divide within them and their ascending and descending branches possess different types of synaptic endings upon the cell bodies of the nuclei.

The secondary fibers take two pathways, both of which run transversely across the medulla oblongata. One part passes through the corpus trapezoideum (Fig. 923, **6, 7**; Fig. 930, *D*), which lies rostrad of the cochlear root and crosses the oblongata dorsally of the deep fibers of the pons. The superior olives and the nuclei of the corpus trapezoideum lie in the course of these fibers and are connected with them by means of collaterals or terminals (Fig. 915, **6**). The other part passes through the striæ medullares acusticæ, which are directed backward and medialward close below the floor of the fourth ventricle (Figs. 903; 905; 914, **16**) to the raphe, to enter the lateral lemniscus of the opposite side. Secondary fibers from the ventral cochlear nucleus take both of these pathways; those from the dorsal nucleus almost all enter the dorsal pathway. Both kinds of fibers connect with the opposite lateral lemniscus, either with or without a synapse in the superior olive (Fig. 930). Collaterals and terminals of these fibers form complicated synapses with the cells of the superior olives and nuclei of the corpus trapezoideum (see Fig. 859). These nuclei send direct tracts to the nucleus of the VI. nerve (Fig. 915, **13**, Fig. 930, *D*) and to other motor nuclei of the oblongata through the formatio reticularis; but most of their fibers accompany the secondary fibers of the corpus trapezoideum to the lateral lemniscus.

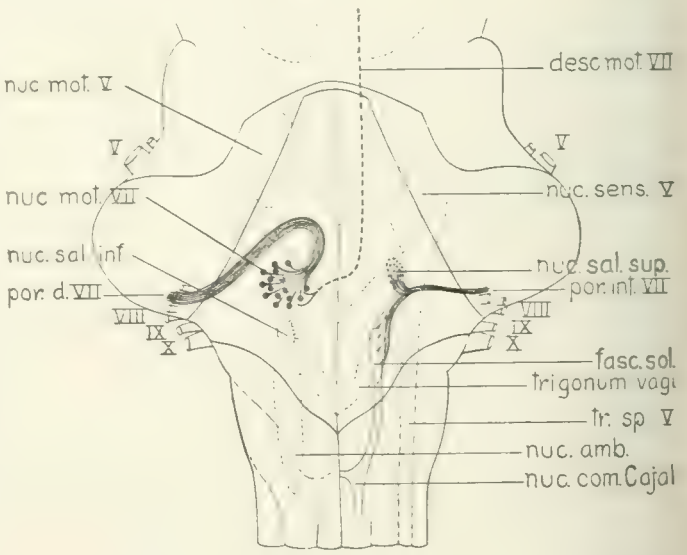

FIG. 927.—Diagram of the Nuclei of the Fascialis Nerve. The portio dura is drawn in on the left side and the portio intermedia of Wrisberg on the right; cf. Fig. 905. *desc. mot. VII.*, Descending tract from cerebral cortex to the motor *VII.* nucleus; *fasc. sol.*, fasciculus solitarius; *nuc. amb.*, nucleus ambiguus; *nuc. com. Cajal*, nucleus commissuralis of Ramón y Cajal; *nuc. mot. V.*, nucleus motorius princeps trigemini; *nuc. mot. VII.*, nucleus motorius princeps facialis; *nuc. sal. inf.*, nucleus salivatorius inferior; *nuc. sal. sup.*, nucleus salivatorius superior; *nuc. sens. V.*, nucleus sensitivus princeps trigemini; *por. d. VII.*, portio dura facialis; *por. int. VII.*, portio intermedia of Wrisberg; *tr. sp. V.*, tractus spinalis trigemini.

The lateral lemniscus contains the great ascending path for cortical acoustic connections. It passes up along the lateral border of the colliculus inferior (Figs. 918, **10, 11**; 922, **8**), where some of its fibers are interrupted in the nucleus of the lateral lemniscus. The remaining fibers pass to the nucleus of the colliculus inferior (Fig. 920, **34**) and to the medial geniculate body (Fig. 919, **8**). There is difference of opinion as to the importance of the colliculus inferior in the

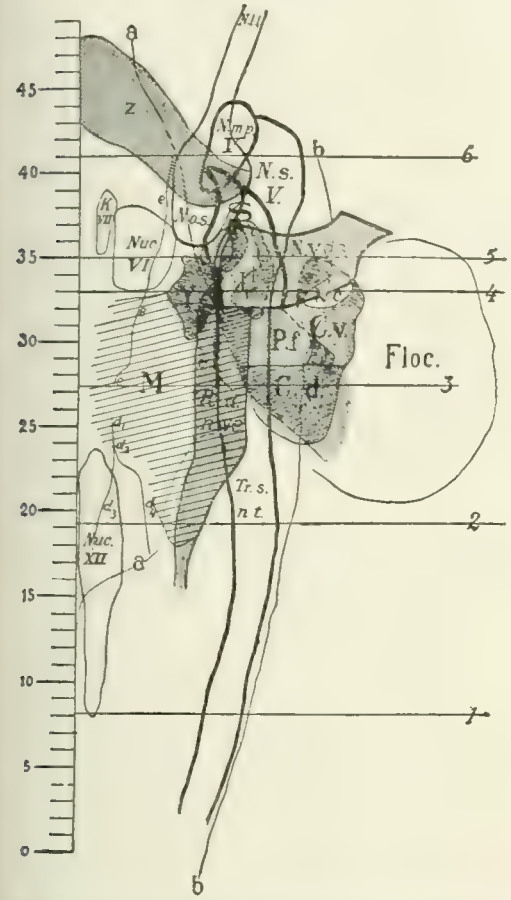

Fig. 928.—Diagram Representing a Flat Reconstruction of the Nuclei of Termination of the Cochlear and Vestibular Nerves in the New-born Babe. The scale at the left is in the median line; the line *a*, *a*, represents the lateral wall of the fourth ventricle; the line *b*, *b*, corresponds to the lateral outline of the corpus restiforme; the line *e*, *e*, *e*, d_1, d_2, d_3, marks the position of the sulcus limitans (cf. Fig. 903). *C.d.*, nucleus nervi cochleæ dorsalis *C.v.*, nucleus nervi cochleæ ventralis; *Floc.*, flocculus; *K. VII.*, knee of the nervus facialis; *L*, medial, and L_1, lateral, portions of nucleus nervi vestibuli lateralis (Deiters); *M.Y.*, nucleus nervi vestibuli medialis (Schwalbe); *N.l.l.*, nucleus of lemniscus lateralis; *Nuc. XII.*, nucleus nervi hypoglossi; *Nuc.VI.*, nucleus nervi abducentis; *P.f.*, pedunculus flocculi; *N.m.p.V.*, nucleus motorius princeps trigemini; *N.o.s.*, nucleus olivaris superior; *N.s. V.*, nucleus sensitivus princeps trigemini; *N.c.*, root bundle of nervus cochleæ; *N.vest.*, root bundle of nervus vestibuli; *R.d.v.ve.*, radix descendens (spinalis) nervi vestibuli; *S*, nucleus nervi vestibuli superior (Bechterew) (area enclosed in the broad black line); *Tr.s.n.t.*, tractus spinalis nervi trigemini; *Y*, anterolateral portion of nucleus nervi vestibuli medialis; *z.*, decussatio nervi trigemini. (After Florence R. Sabin.)

cortical acoustic path. Here important reflex connections are effected and some fibers also ascend through the brachium of the colliculus inferior to the corpus geniculatum mediale. All acoustic fibers are here interrupted, another neurone carrying the impulse upward through the posteroventral part of the internal capsule to the auditory area in the temporal cortex.

The Glossopharyngeal Nerve.—The IX., X., and XI. nerves are intimately related, being the derivatives of the nerves which supply the gills in fishes. The gills are visceral structures and, accordingly, in this part of the body the somatic nerve components and centers are reduced. The sensory and motor roots of these nerves form a linear series which extends backward from the posterior border of the pons into the spinal cord. In the embryo (Fig. 889) the sensory and motor roots lie in separate lines, the ventral, or motor, series extending backward into the spinal cord between the dorsal and ventral roots of the first cervical spinal nerves. In the adult brain the more rostral rootlets belong to the glossopharyngeus, the more caudal rootlets to the accessorius and the intervening ones to the vagus; but it requires a dissection of their peripheral courses to determine the

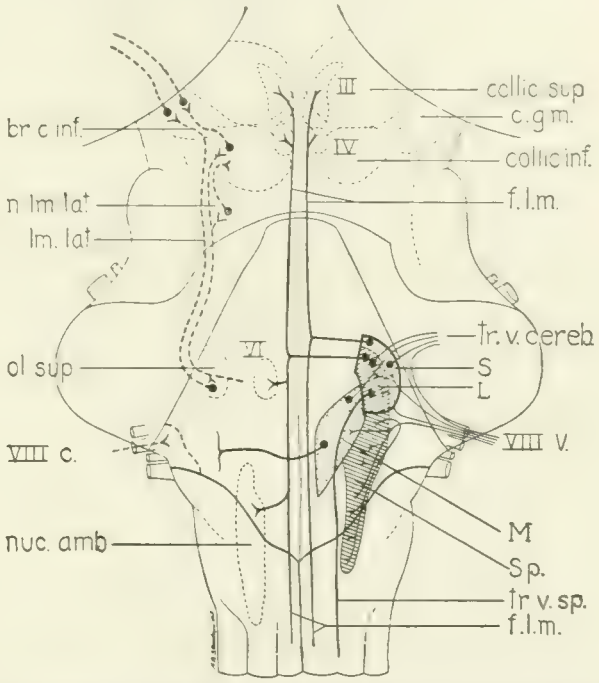

Fig. 929.—Diagram of the nuclei of the VIII. Cerebral Nerve, together with Some of the Associated Fiber Tracts. The secondary tracts associated with the vestibular nuclei are drawn in full lines; those associated with the cochlear nuclei are drawn in broken lines. Cf. Fig. 905. *br. c. inf.*, Brachium of colliculus inferior; *c.g.m.*, corpus geniculatum mediale; *collic. inf.*, colliculus inferior; *collic. sup.*, colliculus superior; *f.l.m.*, fasciculus longitudinalis medialis; *L.*, nucleus nervi vestibuli lateralis (Deiters); *lm. lat.*, lemniscus lateralis; *M.*, nucleus nervi vestibuli medialis (Schwalbe); *n.lm.lat.*, nucleus of lemniscus lateralis; *nuc. amb.*, nucleus ambiguus; *ol. sup.*, oliva superior; *S.*, nucleus nervi vestibuli superior (Bechterew); *Sp.*, nucleus spinalis nervi vestibuli; *tr. v. cereb.*, tractus vestibulo-cerebellaris; *tr. v. sp.*, tractus vestibulo-spinalis; *VIII. c.*, radix cochlearis of VIII. nerve; *VIII. v.*, radix vestibularis of VIII. nerve.

precise limits of these three nerves at their superficial origins from the medulla oblongata.

The IX. nerve contains several components: (1) Somatic sensory fibers supplying general tactile sensibility to the posterior third of the tongue and some neighboring parts. The superior, or jugular, ganglion probably belongs to this component, as is known to be the case in lower vertebrates, and its fibers enter the spinal V. tract (Ramón y Cajal), doubtless terminating in the spinal V. nucleus. (2) Unspecialized visceral sensory fibers probably enter

this nerve from the sympathetic nervous system to end in the nucleus of the fasciculus solitarius. (3) The gustatory fibers of the IX. nerve from the posterior third of the tongue constitute a specialized visceral sensory component. The second and third components are related to the ganglion petrosum and they terminate together in the nucleus of the fasciculus solitarius, which also receives the corresponding roots of the X. nerve. This nucleus accompanies the fasciculus solitarius for its entire length and at its rostral end is expanded to form a more dorsal sensory nucleus under the lateral tip of the trigonum vagi (Fig. 905). (4) The efferent fibers of the IX. nerve are of two sorts. The greater number belong to the specialized visceral motor type, arising from the nucleus ambiguus and distributing to the stylopharyngeus muscle. This is a striated muscle belonging, when phylogenetically considered, to the branchial system. (5) Other efferent fibers belong to sympathetic preganglionic neurones and are excitoglandular in function. These go out by the r. tympanicus glossopharyngei for the innervation of the parotid salivary gland. Their postganglionic neurones probably lie in the ganglion oticum. These preganglionic fibers arise from the nucleus salivatorius inferior, which lies in the reticular formation dorsally of the rostral end of the nucleus ambiguus and ventrally of the dorsal nucleus of the vagus (Yagita). Their position may be seen in Fig. 913 between the points designated **26** and **28**. (6) Other efferent fibers, probably for unstriped muscles, arise from the dorsal vagus nucleus under the trigonum vagi.

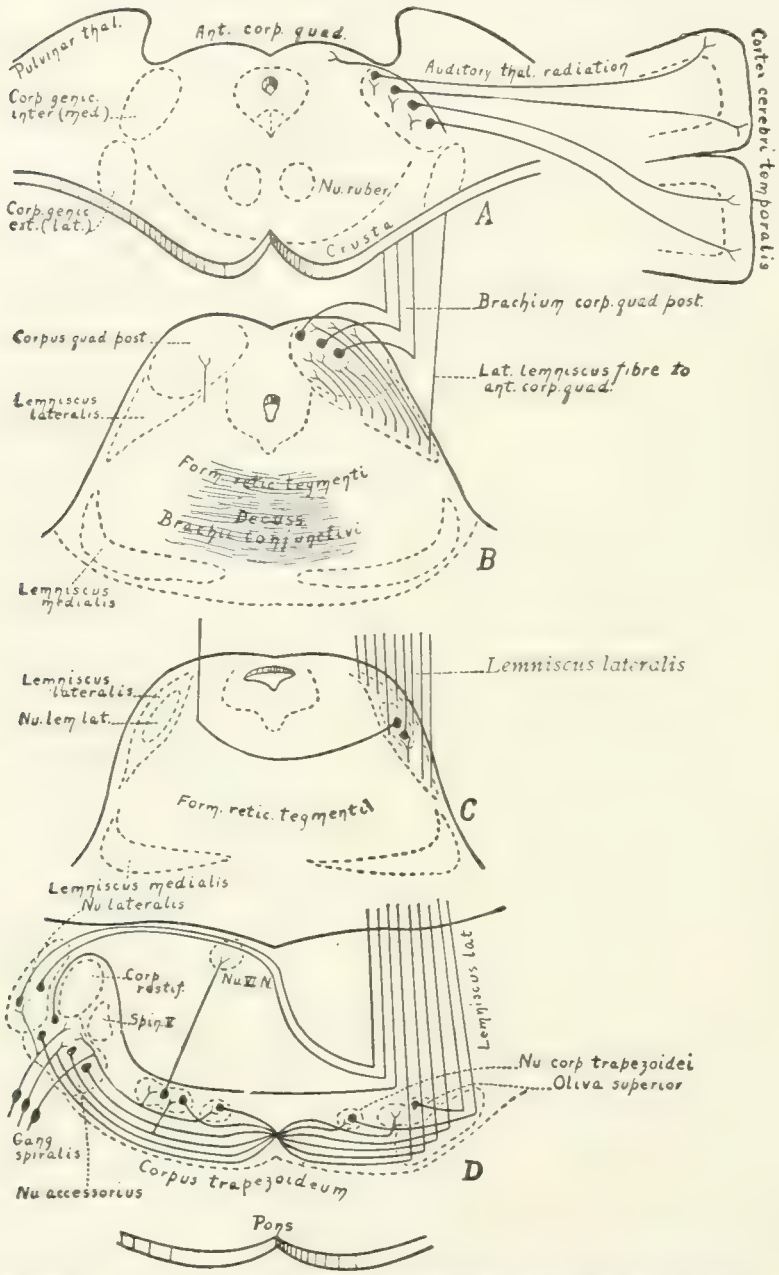

FIG. 930.—Diagram Showing the Connections of the Cochlear Root of the VIII. Nerve. *A*, Section at the level of the colliculus superior and nucleus ruber, showing the auditory radiations from the corpus geniculatum mediale to the temporal cortex cerebri; *B*, section at the level of the colliculus inferior, illustrating the course of the fibers of the brachium of the colliculus inferior (*Brachium corp. quad. post.*) to the medial geniculate body; *C*, section at the level of the nucleus of the lateral lemniscus (*nu. lem. lat.*); *D*, section through the pons at the level of the VIII. roots. In *B* and *C* the basis pedunculi is omitted. (After O. S. Strong, from Bailey's Histology.)

The vagus nerve repeats approximately the same pattern as the IX. nerve, with some important additions. (1) The somatic sensory component is larger, arising from the jugular ganglion and supplying a small area of skin through the r. auricularis vagi. It also terminates in the nucleus of the spinal V. tract. (2) The unspecialized visceral sensory fibers are more numerous, many coming in through the intestinal branch of the vagus, serving general visceral sensations, hunger, thirst, etc. (3) The special visceral sensory component is greatly reduced, but some gustatory fibers are doubtless present for the innervation of the taste buds sparsely scattered over the epiglottis and surrounding regions (J. G. Wilson). The second and third components are related to cells of the ganglion nodosum. (4) The nucleus ambiguus gives rise to a specialized visceral motor component for striated muscles of the visceral (branchial) series in the pharynx, larynx and upper part of the esophagus. (5) The dorsal nucleus of the vagus under the trigonum vagi, or ala cinerea, supplies unspecialized visceral motor (preganglionic) fibers for the cardiac, thoracic and esophageal plexuses, the intestinal nerve and other extensive visceral distributions.

The spinal accessory nerve is a motor nerve whose

fibers are of two sorts. (1) The accessory portion of the nerve is derived chiefly from the nucleus ambiguus; (2) the spinal portion is derived from the cells of the lateral horn of the spinal cord (with which the nucleus ambiguus is directly continuous), as far back as the sixth cervical nerve. The accessory portion is really a part of the vagus, to which it supplies specialized visceral motor fibers, not of sympathetic (preganglionic) type. The spinal portion supplies the fibers to the sternomastoid and trapezius muscles. Sensory fibers in small numbers have been described in the XI. nerve, but these fibers are more commonly regarded as belonging in the vagus.

Summary of the IX., X., *and* XI. *Nerves.*—The arrangement of the roots and nuclei of this group is shown in Fig. 931, and in cross-section in Fig. 884. The few somatic sensory fibers present in these nerves have no separate cerebral centers, but join the spinal V. tract and nucleus. The unspecialized visceral sensory fibers of sympathetic type and the specialized visceral sensory fibers of the gustatory system join those of the VII. nerve in the fasciculus solitarius. Here the gustatory fibers have not been separated from the general visceral fibers, but so far as now known all end together in the nucleus of the fasciculus solitarius and a closely associated dorsal sensory nucleus which lies under the lateral part of the trigonum vagi. The fasciculus solitarius, accompanied by its nucleus, extends downward into the spinal cord. A short distance below the calamus scriptorius a part of its fibers enter a dorsal commissure and cross to the other side. Embedded within this commissure is a nucleus which receives terminals of the root fibers of the IX. and X. nerves. The commissure has long been known to occur in fishes, where it was named the commissura infima by its discoverer, A. von Haller. The connection of the commissure with the fasciculus solitarius and the presence of the nucleus were discovered by Ramón y Cajal and the nucleus is termed the commissural nucleus of Cajal.

The visceral sensory nucleus associated with the fasciculus solitarius effects numerous reflex connections with the reticular formation and motor centers of the oblongata. Its cerebral path to the cortex is wholly unknown in mammals. In fishes there is a large uncrossed ascending pathway for gustatory impressions which reaches a nucleus under the cerebellum near the decussation of the IV. nerve. Here there is a partial decussation and a synapse. The gustatory neurone of the third order passes from this nucleus to the hypothalamus.

The nucleus ambiguus is the cerebral extension of the lateral horn of gray matter of the spinal cord, and not of the ventral horn, as is often stated. Its neurones belong to the lateral series of nuclei of the oblongata (represented in the XI., X., IX., VII. and V. nerves (cf. Fig. 905), which supply chiefly striated visceral muscles and belong to the specialized visceral motor system. Some root fibers cross in the ventral raphe to terminate in the nucleus ambiguus of the opposite side. The precise course of the cortical motor path to this nucleus is not known. The unspecialized (preganglionic) visceral components of these nerves arise for the most part from nuclei containing smaller cells which lie farther dorsally—the dorsal motor X nucleus under the caudal part of the trigonum vagi and the nucleus salivatorius inferior. The nucleus salivatorius superior and the small-celled III. nucleus also belong in this series. The dorsal nucleus of the vagus has until recently been commonly regarded as sensory. In 1891 Forel, and after him many others, have presented experimental evidence of its motor character. It is certainly not a homogeneous nucleus, and its lateral part appears to belong with the nucleus of the fasciculus solitarius as a visceral receptive center.

The hypoglossus nerve is a simple somatic motor nerve. Its nucleus is the morphological extension of the ventral horn of the spinal cord, and in lower vertebrates these are directly continuous. Fishes, in fact, have no separate XII. nerve, but the tongue musculature is innervated by branches of the ventral roots of the first spinal nerves. In higher forms the sensory roots of these nerves are lost and the nervus hypoglossus is the survivor of the ventral roots of one or more of these modified segmental nerves. Parallel with this evolutionary history, the hypoglossus nucleus has migrated from a ventral position in lower animals to its place immediately below the floor of the fourth ventricle, and also considerably farther forward, so that the hypoglossus lies in the same transverse plane as the vagus. Thus, the tongue musculature is brought into closer physiological relations with the sensory nuclei of the gustatory system of the VII. and IX. nerves (Kappers). See Figs. 905, 912, 920, 922, 923.

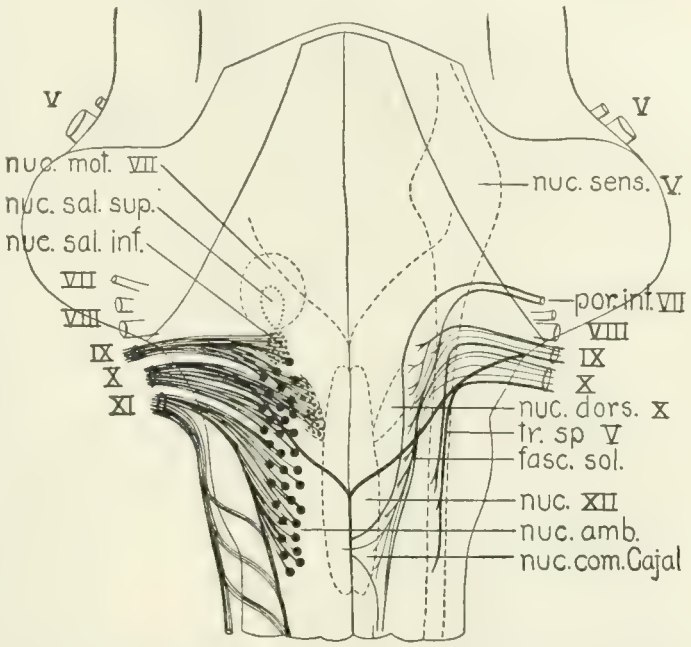

FIG. 931.—Diagram of the Roots and Nuclei of the IX., X., and XI. Cerebral Nerves. The motor roots are drawn in on the left side; the sensory roots on the right side. Cf. Fig. 905. *fasc. sol.* Fasciculus solitarius; *nuc. amb.*, nucleus ambiguus; *nuc. com. Cajal*, nucleus commissuralis of Cajal; *nuc. dors.* X., nucleus dorsalis vagi; *nuc. mot. VII.*, nucleus motorius princeps facialis; *nuc. sal. inf.*, nucleus salivatorius inferior; *nuc. sal. sup.*, nucleus salivatorius superior; *nuc. sens. V.*, nucleus sensitivus princeps trigemini; *nuc. XII.*, nucleus hypoglossi; *por. int. VII.*, portio intermedia (Wrisbergi) facialis; *tr. sp. V.*, tractus spinalis trigemini.

The hypoglossus nucleus receives important tracts from the nucleus of the fasciculus solitarius and from the reticular formation for short reflexes connected with the cerebral nerves. The cortical path arises from the opercular part of the frontal lobe, passes downward through the genu of the internal capsule into the pyramidal tract, whose most medial fibers it forms (Fig. 934, *Tr. cort.-bulb. m.*), then below the pons it bends dorsalward to cross the raphe and enter the XII. nucleus from the lower and inner side.

The Formatio Reticularis.—The nuclei of the cerebral nerves which have been enumerated above constitute the primary intrinsic sensori-motor apparatus of this region. Between these nuclei lies the reticular substance, by means of whose neurones the various reflex arcs with which these primary centers are concerned are completed. The olivary nuclei, the pontile nuclei, the arcuate nucleus and some other especially elaborated gray centers represent more highly differentiated areas within the reticular formation, whose connections will be taken up in more detail beyond. The cerebellum is an extensive suprasegmental apparatus developed from this region to serve the proprioceptive functions of equilibration and muscular coordination, largely or wholly on the reflex or involuntary plane.

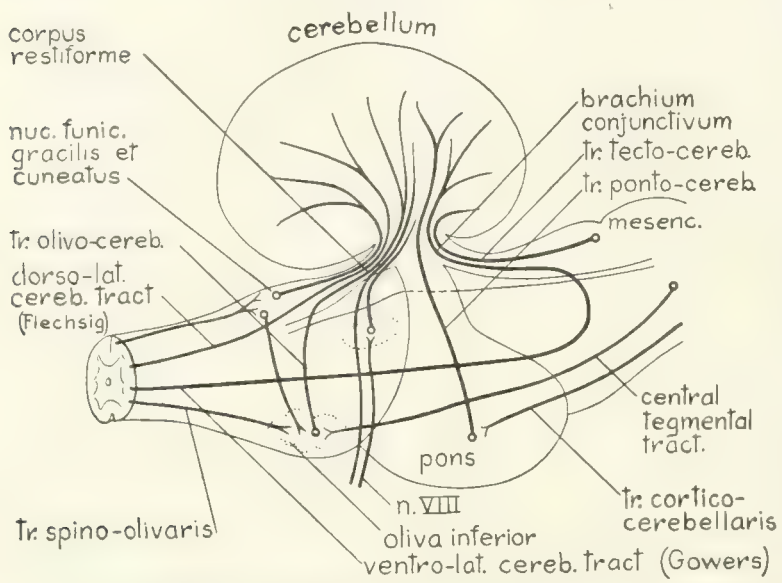

Fig. 932.—Diagram of the Chief Afferent Tracts Connected with the Cerebellum.

The Cerebellum.—To the metencephalon, as this term is here used, belong the cerebellum (epencephalon), pons, brachium pontis, and nuclei pontis. These constitute a functional unit, which is related by means of afferent and efferent fiber tracts with all parts of the brain stem which are concerned with the proprioceptive reflexes, and also with the cerebral cortex. The brain stem connections are the more primitive and are related to the central cerebellar mass, the vermis, while the larger cerebellar hemispheres, the pons, pontile nuclei and brachium pontis are connected by way of the cortico-pontile tracts and the pyramidal tract with the cerebral cortex. Except for this difference in the fiber connections of the cerebellar hemispheres and vermis, the cerebellar cortex exhibits no structural or physiological evidence of localization of diverse functions in different parts, such as characterizes the cerebral cortex; accordingly we shall not here enter into a description of its anatomical subdivisions. The deeper gray masses within the cerebellum, however, are functionally diverse. There are two groups of such gray masses, first, the roof nuclei in the vermis, immediately above the fourth ventricle, and second the dentate nucleus farther laterally. The cerebellum is connected with the brain stem by three peduncles, the anterior (brachium conjunctivum) and posterior (corpus restiforme) being connected chiefly with the vermis, and the middle peduncle (brachium pontis) putting the cerebellar hemispheres into relation with the pons and its nuclei.

The accompanying schemata (Figs. 932, 933) illustrate the chief systems of afferent and efferent tracts connected with the cerebellum. It will be noticed that the entire somesthetic system of the body (both cutaneous and deep sensibility) may discharge impulses into the cerebellum by way of the restiform body and brachium conjunctivum and that the vestibular nerve is in especially close physiological connection with it. In lower vertebrates tnere is a strong direct connection from the optic centers of the midbrain to the cerebellum (tractus tectocerebellaris). This connection is reduced in man (though still present, as Edinger has recently shown), probably being functionally replaced by the midbrain-olivary path to the cerebellum and by cortical connections. The inferior olive receives ascending fibers from the whole length of the spinal cord (Goldstein), descending fibers from the optic tectum of the midbrain (by the central tegmental tract) and fibers from the nuclei of the funiculi gracilis and cuneatus of the opposite side. It is connected with the cerebellum through the restiform body of the opposite side, these fibers probably running in both the ascending and descending direction.

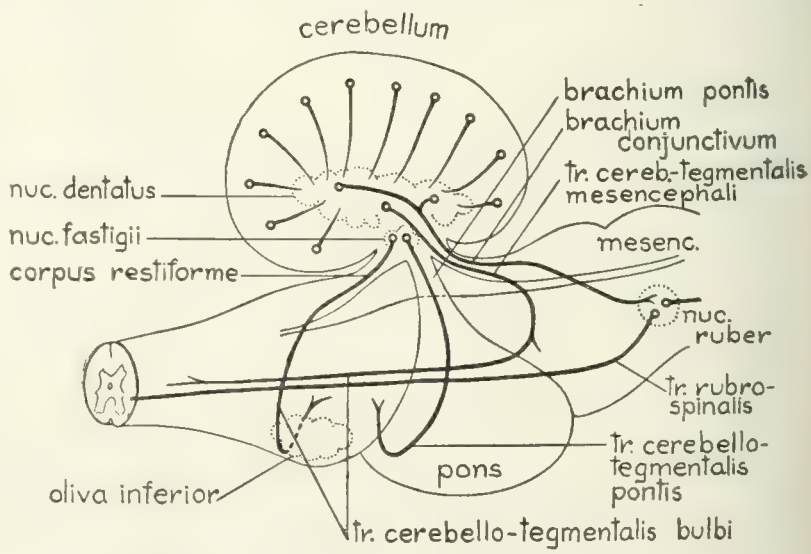

Fig. 933.—Diagram of the Chief Efferent Tracts Connected with the Cerebellum.

The fibers from the cerebral cortex to the cerebellum constitute two chief tracts, the frontal corticopontile

tract, passing through the midbrain medially of the pyramidal tract, and the temporal corticopontile tract, passing laterally of the pyramidal tract (cf. Fig. 934). Some fibers probably come from the occipital part of the cerebral hemisphere, and collaterals are given off to the pontile nuclei from the pyramidal tract itself. After a synapse in the pontile nuclei, these corticopontile tracts effect functional connections through the brachium pontis, chiefly with the cerebellar hemisphere of the opposite side. The brachium pontis also carries descending impulses from the cerebellar hemispheres to the tegmental nuclei. The other descending fibers from the cere-

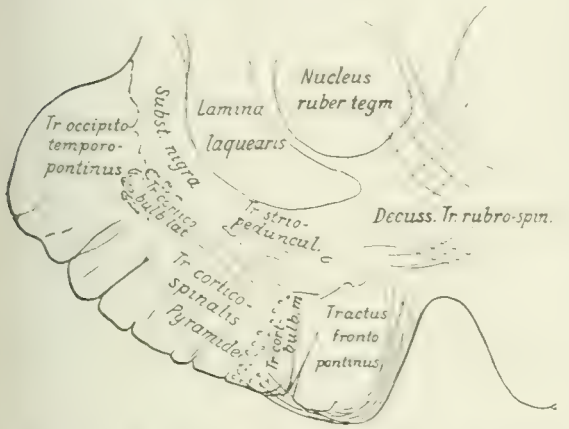

Fig. 934.—Diagram of the Basis Pedunculi of the Human Brain Showing the Localization of its More Important Fiber Systems. (After Edinger.)

bellum pass out chiefly through the brachium conjunctivum to the red nucleus, tegmentum and thalamus of the opposite side (Fig. 893).

The roof nuclei in the vermis are the nuclei fastigii, emboliformis and globosus. Situated more laterally in the core of the white substance of each hemisphere is the nucleus dentatus. The efferent fibers of the cerebellum arise as axons of the Purkinje cells of the cerebellar cortex, and those from the hemispheres terminate in the dentate nuclei, while those from the vermis terminate chiefly in the roof nuclei. The latter also receive some afferent fibers from the spinal cord and brain stem. The cells of the dentate nucleus give rise to most of the fibers of the brachium conjunctivum.

The cerebellar cortex is structurally similar throughout the whole of this organ. External to the central white matter, which composes the so-called arbor vitæ, there is a wide granular layer, composed of very minute granule cells densely crowded together, with scanty cytoplasm, short claw-like dendrites and slender unmedullated axones which ascend to the superficial layer, where they bifurcate and end among the dendrites of the Purkinje cells. The middle layer is composed of a single series of Purkinje cells. These cells have large, globose bodies with massive bushy dendrites directed outward and slender axones directed inward. These axones soon acquire medullated sheaths and form the chief efferent pathway from the cerebellum. The outermost, or molecular, layer contains the dendrites of the Purkinje cells, termini of the axones of the granule cells and of other fibers and a small number of correlation neurones of several types, among which are the basket cells illustrated in Fig. 860. These relations are shown schematically in Figs. 935 and 936. Afferent fibers terminate in the cerebellar cortex in two ways. They may pass directly out to the molecular layer as climbing fibers (Fig. 936, *n*), where they end in very intimate relation with the dendrites of the Purkinje neurones, or they may end as mossy fibers (Fig. 936, *h*), among the cells of the granular layer. Here the granule cells take up the impulse and deliver it to the dendrites of the Purkinje cells, as shown in Fig. 935. By this means, as well as by the basket cells and other types of association neurones, a single incoming nerve impulse may be distributed to many Purkinje neurones and thus its physiological effect be greatly enhanced. The same result is also secured by the discharge of collateral fibers from the Purkinje cell axones as they pass through the granular layer, thus providing for summation and reinforcement of stimuli during the process of transmission through the cerebellar cortex. This type of discharge has been termed by Ramón y Cajal "avalanche conduction," and plays a very important rôle in many parts of the central nervous system. Golgi believes that these collateral branches of the Purkinje axones anastomose with each other within the granular layer to form a true rete nervosa diffusa, thus permitting the efferent impulse to be diffused very widely in this layer. Whether the fibers which compose this neuropil are in actual physical connection or not, our present technical methods are not adequate to decide; but the physiological effect referred to above would be possible in either case.

The Mesencephalon.—The general form of the midbrain is seen in Fig. 937. The dorsal surface is marked by the superior and inferior colliculi. The latter, as we have seen, has been differentiated to serve as a reflex center interpolated in the cortical acoustic path. The superior colliculus serves chiefly as a center for optic reflexes. Ventrally of the aqueduct of Sylvius (see Fig. 919) are found the motor nuclei of the III. and IV. cerebral nerves; the nucleus ruber which is the chief center for the dis-

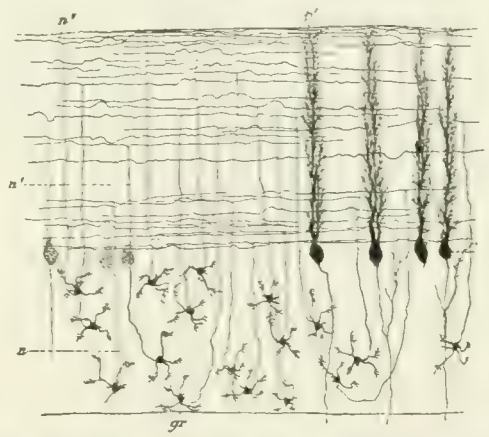

Fig. 935 Section Through the Cerebellar Cortex taken Parallel with the Long Axis of a Lamina. Comparison with Fig. 936, taken transversely to a lamina, illustrates the broad but thin expanse of the dendrites of the Purkinje neurones and the way in which each of these is spread out so as to come into contact with the largest possible number of axones of the granule cells in the molecular layer. *gr.*, Cell of the granular layer; *n.*, axone of granule cell; *n'*, same in molecular layer, where it branches and both branches run parallel with the long axis of the lamina; *p.*, Purkinje cell, with its dendrite, *p'*, spreading but slightly in the long axis of the lamina. Golgi method. (After Kölliker, from Bailey's Histology.)

tribution of efferent cerebellar impulses; the substantia nigra which is motor correlation tissue interpolated between the ascending lemniscus systems and the descending systems associated with the pyramidal tracts; the medial and lateral lemniscus; and the descending fibers along the ventral surface which compose the basis pedunculi, pes pedunculi or crusta. The region between the gray masses of the superior and inferior colliculi (corpora quadrigemini) and the substantia nigra is termed the tegmentum. It is a continuation of the ret-

icular formation of the medulla oblongata and contains, in addition to innumerable short reflex con-

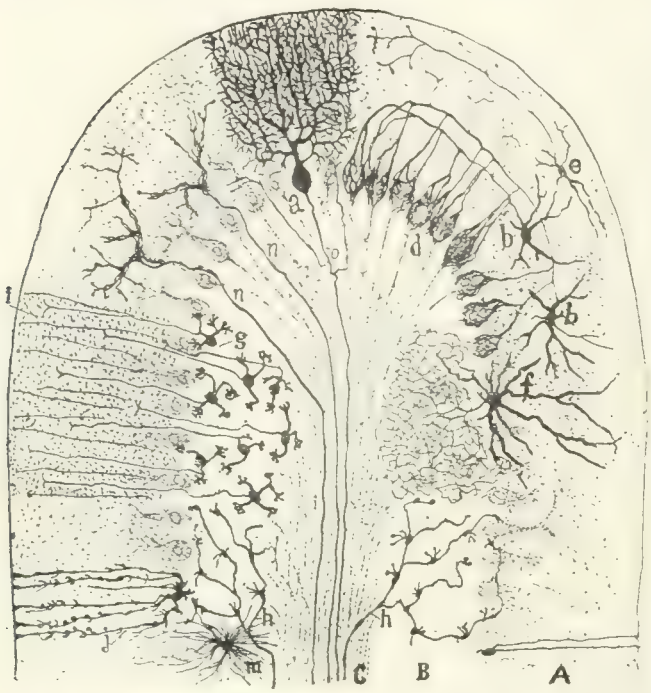

FIG. 936.—Semidiagrammatic Section taken Transversely through a Lamina of the Cerebellar Cortex. Golgi method. *A*, Molecular layer, filled with axones of granule cells cut at right angles to their course; *B*, granular layer; *C*, white matter; *a*, Purkinje cell, with the dendrite broadly spread out in the transverse plane (cf. Figs. 862 and 935); *b*, basket cell (cf. Fig. 830); *d*, terminal arborizations of the basket cells enveloping the bodies of the Purkinje cells; *e*, superficial stellate cells; *f*, Golgi cell of type II.; *g*, granule cells with their axis cylinders ascending and bifurcating in the molecular layer at *i*; *h*, mossy fibers; *j*, neuroglia cell; *m*, neuroglia cell; *n*, climbing fibers. (After Ramón y Cajal, from Bailey's Histology.)

nections, several long conduction paths, such as the lemniscus system, the brachium conjunctivum, fasciculus longitudinalis medialis, etc. The latter is a strong tract which extends from a nucleus at the upper end of the midbrain throughout the entire length of the brain stem and downward into the fasciculus proprius ventralis of the spinal cord. It contains both ascending and descending fibers, most of which run a short course and coordinate the reactions of the motor nuclei. Some, however, run a longer course and carry impulses from the brain stem to the motor centers of the spinal cord.

The Diencephalon.—Immediately in front of the superior colliculus the brain stem expands laterally to form the thalamic nuclei (Figs. 938 and 975). The diencephalon, as we have already seen, consists of three primary divisions, the epithalamus, the hypothalamus and the thalamus proper (including the metathalamus of His)

The investigation of the functional connections of the diencephalic nuclei is beset with many difficulties, and the subject is still in some confusion. Thalamic lesions, whether produced experimentally or by pathologic processes, are apt to injure also some of the systems of long conduction paths passing through the thalamus and the symptom-complex is thus complicated by the involvement of disturbances of remote parts of the brain which have no important functional relations with the diencephalon.

The Thalamus.—The connection of the epithalamus and hypothalamus are discussed beyond in connection with the rhinencephalon. The thalamus proper, as has been pointed out in the second section of this article, is devoted to sensori-motor correlation (somatic systems chiefly) and to the transmission of somatic sensory impulses forward into the cerebral cortex. The intrinsic, *i.e.* non-cortical, connections of the thalamus are performed by the more medial thalamic nuclei; the cortical connections are effected chiefly by the lateral and ventral groups of nuclei. The thalamus is divided functionally into a pars dorsalis, which is composed of afferent correlation centers, and a pars ventralis, composed of efferent correlation centers. The relations of these parts are much more clearly seen in some lower vertebrates, like the tailed Amphibia, where the cerebral cortex is feebly developed and the primitive relations of the intrinsic thalamic centers are not complicated by large cortical dependencies, as in man.

In Necturus, the common "mud puppy," for instance, the cerebral hemispheres are devoted chiefly to the primary olfactory apparatus and various centers for the correlation of this with other sensory areas (Fig. 939). An examination of the ventricular surface of the diencephalon and mesencephalon of Necturus (Fig. 940) shows that the hypothalamus, the preoptic nuclei (pars optica hypothalami, His) and the epithalamus (habenula) are highly developed, these being the chief avenues of discharge and correlation between the olfactory association centers of the hemispheres and the tegmentum. In the thalamus the pars dorsalis is very rudimentary, while the pars ventralis is very large, this being the converse of the relation between these parts in higher vertebrates. The caudal end of the pars ventralis thalami clearly lies below the sulcus limitans in the primary ventrolateral or motor lamina, but its rostral end extends forward across the site of the sulcus limitans (which is here obliterated) into the primitive sensory lamina. This secondary enlargement of the pars ventralis by the en-

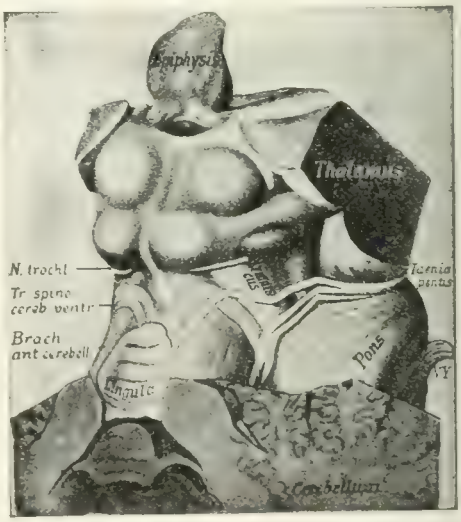

FIG. 937.—View of the dorsal Surface of the Midbrain. (After Retzius, from Edinger's Vorlesungen.)

croachment of tissue of the motor type into the dorsolateral lamina arises from the fact that the pars ventralis thalami in this animal receives a large

proportion of the efferent fibers from the midbrain and thalamus (chiefly by way of the tracts of the postoptic decussation) and then transmits these impulses by descending tracts into the motor centers of the tegmentum. Fig. 941 illustrates the typical arrangement of these tectothalamic and thalamopeduncular tracts, this being the primitive correlation mechanism of the somatic sensory systems in animals lacking a differentiated cerebral cortex.

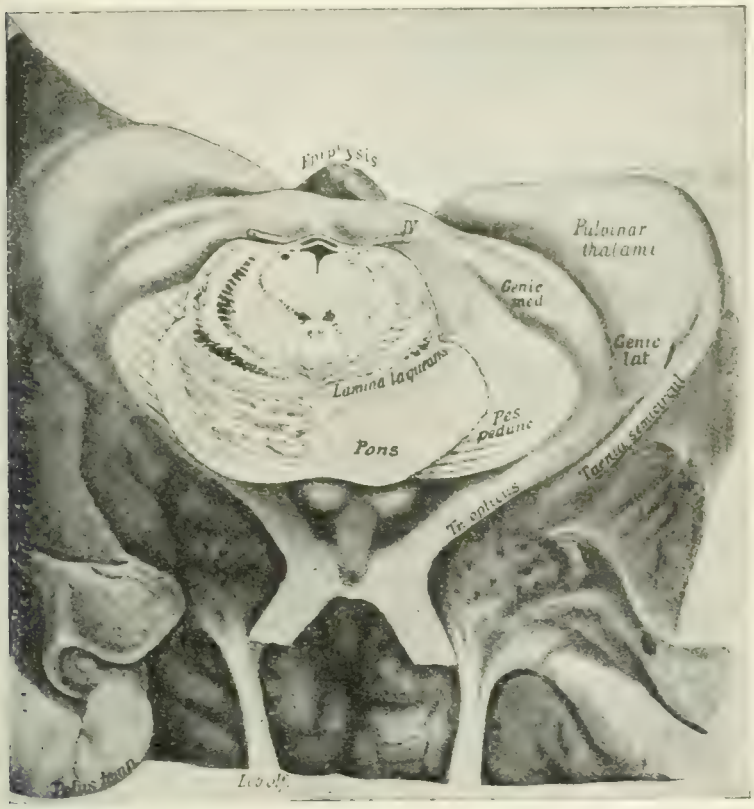

Fig. 938.—View of the Brain as Seen after Cutting it Transversely through the Pons at the Level of the Exit of the IV. nerves. The relations of the medial and lateral olfactory striæ to the area olfactoria are clearly shown. (After Edinger.)

But in Necturus the beginnings of the cerebral cortex have already appeared and the somatic sensory correlation centers in the pars dorsalis thalami send small but clearly defined sensory radiations into the cerebral hemisphere, as shown in Fig. 942. The return pathway for corticospinal impulses of this system passes through the ventral part of the thalamus. Here some of its fibers end, but most of them pass farther back into the pedunculus cerebri and tegmentum of the midbrain. The dorsal part of the thalamus is, then, a sort of vestibule where tactile, acoustic, optic, and other somatic sensory impressions are received and then transmitted forward to the cerebral cortex; the ventral part, on the other hand, is adapted to receive the same somatic sensory impulses and transmit them directly backward into the motor centers.

In higher vertebrates, parallel with the evolution of non-olfactory somatic sensory correlation centers in the cerebral cortex (neopallium), the pars dorsalis thalami assumes relatively greater importance, while the pars ventralis shrinks into relative insignificance. In mammals the chief function of the latter seems to be to receive collateral discharges from the descending cortical fibers of the pyramidal tract (Ramón y Cajal), where they doubtless reinforce the reflexes effected within the thalamus by surviving vestiges of the intrinsic primitive reflex thalamic connections which constitute the chief part of the thalamus in the Amphibia. The recent researches of Head and Holmes (1911) make it evident that even in man the thalamus has important functions quite independently of the cerebral cortex.

In the embryonic human brain the same elementary subdivision of the thalamus is evident in early stages. The sulcus limitans (marked sulcus hypothalamicus on Fig. 896) is visible throughout the entire prosencephalon in an embryo of five weeks. It turns ventrally into the preoptic recess in such a way as to leave the entire hypothalamus and a small part of the thalamus on its ventral side, while the greater part of the thalamus and all of the epithalamus lie dorsally of it. The pars dorsalis thalami lies immediately in front of the tegmental swelling shown in Fig. 896, and here, as in Necturus, some of the tissue of the primary dorsal lamina which lies immediately in front of the primary motor part of the thalamus and between the recessus preopticus and the sensory thalamic centers (Fig. 896) seems secondarily to have acquired the same character as the adjacent motor lamina, *i.e.* it has become an efferent center discharging directly into the tegmentum; it, therefore, must be joined functionally to the pars ventralis thalami.

The sensory correlation centers which constitute the remainder of the thalamus discharge forward into the cerebral hemisphere, these fibers comprising the great sensory radiations into the cerebral cortex. The pars dorsalis thalami contains a medial group of relatively unspecialized nuclei (intrinsic apparatus of the thalamus devoted to thalamic reflexes), the great nucleus sensitivus (Ramón y Cajal)

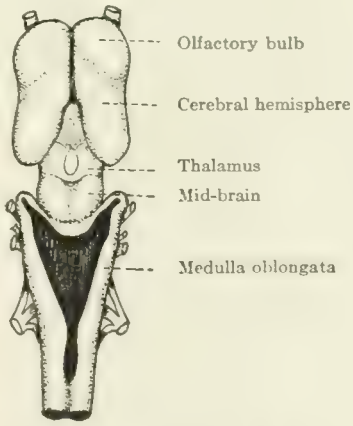

Fig. 939.—Dorsal View of the Brain of Necturus maculatus. × 2⅞.

or lateral nucleus which receives lemniscus fibers for tactile and general sensibility, the lateral geniculate body and pulvinar for optic impulses, the medial gen-

iculate body for acoustic impulses, and some other sensory correlation centers, all of which are in intimate relation with the cerebral hemispheres. The two geniculate bodies comprise the metathalamus of His. The pars ventralis thalami (including its secondary forward extension described in the last paragraph) occupies the regio subthalamica, which

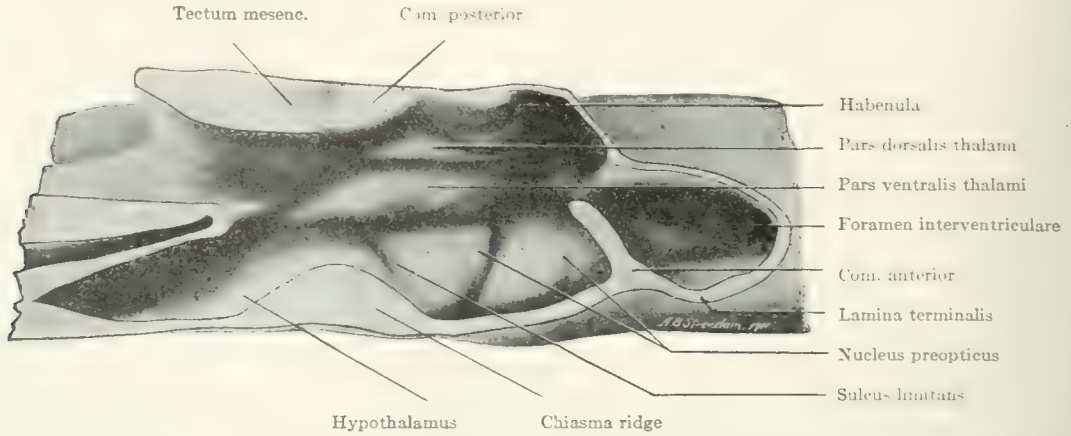

Fig. 940.—View of the Left Half of the Midbrain and Thalamus of Necturus after Vertical Medial Section of the Brain, seen from the Ventricular Surface, to Illustrate the Relations of the Dorsal and Ventral Parts of the Thalamus. × 13. After McKibben (Journal of Comparative Neurology, Vol. 21, p. 283, 1911).

is often erroneously joined to the hypothalamus, and which contains a part of the zona reticularis (lattice nucleus or Gitterschicht), the nucleus hypothalamicus of Luys, and other gray centers of the same intermediary motor type as the substantia nigra in the tegmentum (cf. Ramón y Cajal, 1911, p. 501–503).

In the brains of late embryos and adults the thalamus is separated from the hypothalamus and pars

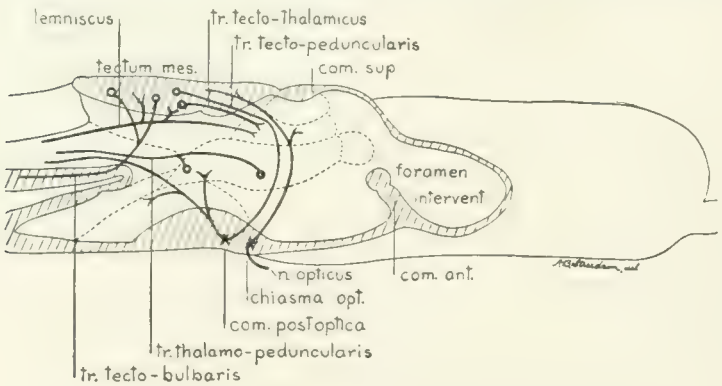

Fig. 941.—Diagram based on Fig. 940 to Illustrate Some of the Intrinsic Subcortical Reflex Pathways of Necturus. The Lemniscus and optic tract discharge chiefly into the tectum mesencephali, but partly into the dorsal part of the thalamus. The return motor pathway from the tectum follows two main lines: (1) the tractus tecto-bulbaris to the motor centers of the medulla oblongata and spinal cord, part of these fibers decussating in the ventral commissure of the tegmentum; and (2) the tractus tecto-peduncularis. The latter tract, after decussating in the postoptic commissure, discharges in part into the tegmentum, in part into the hypothalamus, and in part into the pars ventralis thalami, from which the tractus thalamo-peduncularis transmits the impulse to the tegmentum.

optica hypothalami (preoptic nucleus) by a well-defined sulcus which extends backward from the interventricular foramen to the aqueduct of Sylvius (visible but not labelled in Fig. 892). This sulcus was first recognized by Reichert and named by him (1861) sulcus Monroi, a name which has since been applied to other sulci by different authors, *e.g.* by His, who gives this name to the rostral end of the sulcus limitans. The latter is called sulcus hypothalamicus by Spalteholz in his reproductions of the figures of His which are copied in this article. The pars ventralis thalami of the adult human brain is not represented on the ventricular surface, but has receded laterally along the line of the sulcus Monroi of Reichert. The geniculate bodies of the pars dorsalis thalami (metathalamus of His) have also been carried laterally in the position of the caudal end of this sulcus (Figs. 891, 892).

The synonymy of the thalamic nuclei is in great confusion. Here we shall follow the classic description of von Monakow, whose analysis of the thalamic centers is illustrated in Figs. 943 to 947.

In Fig. 943, which represents a transverse section through the human brain at the level of the decussation of the brachium conjunctivum, the three nuclei of the metathalamus are seen (pulvinar, medial and lateral geniculate bodies) and also the nucleus posterior thalami. The position of the lemniscus is also indicated (S_1, S_2). Lateral and dorsal from the lemniscus is the brachium quadrigeminum inferius or arm of the inferior colliculus, which is a link in the acoustic pathway between the inferior colliculus and the medial geniculate body.

A section farther forward through the upper border of the superior colliculus (Fig. 944) shows, in addition to the structures just mentioned, the lateral part of the nucleus ventralis thalami, to which some of the ascending fibers of the lemniscus are given off.

Fig. 945 passes through the middle of the thalamus. The tænia thalami marks the line of attachment of the membranous roof of the third ventricle, which has been removed. The tænia is accompanied by a tract of medullated fibers, the stria medullaris thalami, by which the olfactory centers of the cerebral hemisphere discharge into the epithalamus, or habenula, which in sections farther back would be seen lying immediately caudad of the tænia thalami as here figured; cf. Fig. 948. The hypothalamus does not appear in this figure, lying farther forward. The regio subthalamica at this level includes the corpus Luysi (here termed "nucleus hypothalami-

cus," though it does not properly belong in the hypothalamus). The ventral and medial nuclei of the thalamus are shown; also the caudal end of the

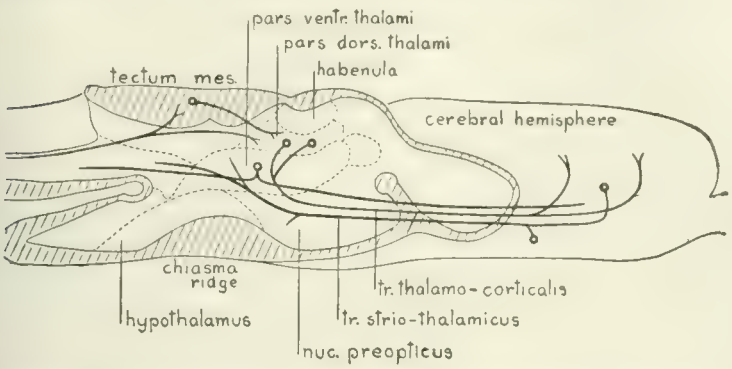

FIG. 942.—A Diagram Similar to that of Fig. 941, to Illustrate the Connections of the Pars Dorsalis Thalami of Necturus. This part receives somatic sensory fibers from the lemniscus and from the tectum mescephali and its chief discharge pathway is by the tractus thalamo-corticalis to the cerebral hemisphere. This path is the precursor of the great thalamo-cortical sensory radiations of mammals.

lateral nucleus, though this is not named on the figure. The lemniscus fibers have terminated in large numbers in the ventral nucleus; other fibers of this system are represented in the lamina medullaris medialis for levels farther forward. The fibers of the basis pedunculi now lie farther lateralward nearer the internal capsule, within which they are found in the next section figured. Numerous fibers are seen passing from the lateral border of the thalamus into the internal capsule. These are sensory radiations, or thalamo-cortical tracts, of the optic, acoustic and tactile systems from their respective thalamic centers.

Fig. 946 illustrates a section taken immediately behind the optic chiasma. The greater part of the hypothalamus (mammillary bodies and tuber cinereum) lies between this level and that of Fig. 945, but the rostral end of it is seen lying between the tractus opticus and Forel's Feld H_2. The latter lies in the subthalamic region (pars ventralis thalami). In the pars dorsalis thalami, are seen, passing from the third ventricle lateralward, the tenia thalami (which with the accompanying stria medullaris is the only representative of the epithalamus at this level), the nucleus medialis thalami (not named on the figure), the lamina medullaris medialis, the nucleus anterior thalami, the nucleus lateralis thalami and the zona reticularis. Lateral from the latter is seen the capsula interna. The anterior part of the nucleus ventralis thalami is met with in the ventral part of the thalamus. At the ventral extremity of the lamina medullaris medialis, in transverse section, is seen the fasciculus thalamomammillaris (of Vicq d'Azyr, better named the tractus mammillo-thalamicus), which puts the hypothalamus into relation with the nucleus anterior thalami. In the hypothalamus is seen the columna fornicis, which conducts from the olfactory cerebral cortex (hippocampus) to the mammillary body in the hypothalamus. Surrounding it, but not shown on the figure, are fibers of the basal olfactory tract which carries subcortical olfactory impulses from the basal olfactory centers to the hypothalamus (cf. Figs. 948, 973).

Fig. 947 passes through the most rostral portion of the thalamus. Passing from the middle line lateralward are seen the stratum griseum centrale, the tenia thalami, the nucleus anterior thalami with its ventral capsule, the tractus mammillo-thalamicus (Vicq d'Azyri), the nucleus lateralis thalami, and the nucleus

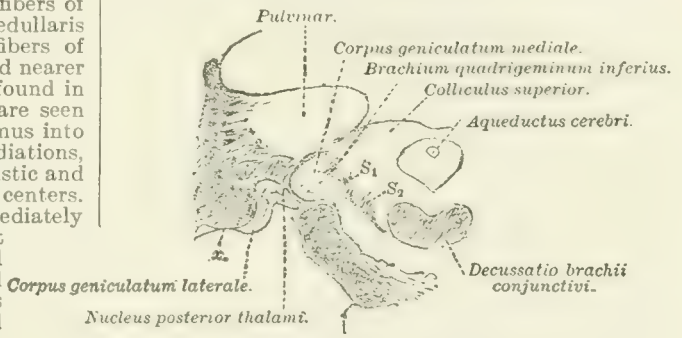

FIG. 943.—Frontal Section through a Normal Human Brain at the Level of the Decussatio Brachii Conjunctivi. (After C. von Monakow, *Arch. f. Psychiat.*, Berlin, Bd. xxvii., 1895.) S_1, S_2, Lemniscus. (From "The Nervous System and Its Constituent Neurones," New York, 1900.)

ventralis thalami (anterior part). Bounding the thalamus lateralward is the capsula interna of the corpus striatum. The three parts of the nucleus lentiformis of the corpus striatum are represented, namely, the pars medialis and the pars lateralis of the globus pallidus and the putamen. Ventral to the globus pallidus is the commissura anterior cerebri. The pedunculus thalami medialis carries fibers between the basal olfactory centers lying farther forward and the medial group of nuclei of the thalamus, which at this level are represented by the stratum griseum centrale and the nucleus anterior.

In these figures it will be observed that the sensory nuclei of the thalamus (pars dorsalis thalami of this article) tend to be arranged in concentric fashion around the third ventricle and that they fill almost the entire thalamus. This part includes the nucleus anterior (nucleus dorsalis of many authors), nucleus medialis, nucleus lateralis, nucleus ventralis, nucleus posterior and the metathalamus of His (lateral and medial geniculate bodies and pulvinar). Each of these nuclei has a

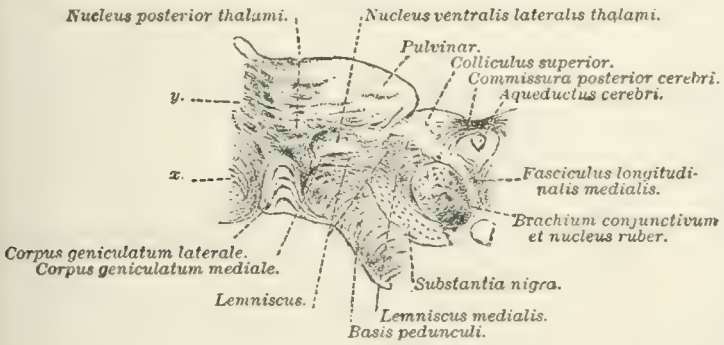

FIG. 944.—Frontal Section through a Normal Human Brain at Level of Upper Extremity of Corpus Geniculatum Mediale. (After C. von Monakow, *Arch. f. Psychiat.*, Berlin, Bd. xxvii., 1895, Taf. ii., Fig. 13.) *x*, Lateral white matter of lateral geniculate body; *y*, lateral white matter of pulvinar. (From "The Nervous System and Its Constituent Neurones," New York, 1900.)

characteristic form and arrangement of its neurones and is more or less clearly separated from its neighbors by laminæ of medullated nerve fibers. The suggestion that they are functionally different is confirmed by the limited data from physiological experiments and pathological cases available. The medial nuclei, as elsewhere in the brain, are the more primitive centers and serve the simpler intrinsic thalamic reflexes. The nuclei of the metathalamus serve as cortical dependencies of the more highly differentiated functions of sight and hearing, while the intervening lateral and ventral nuclei are for the most part similar cortical dependencies of the tactile and somesthetic sensory systems.

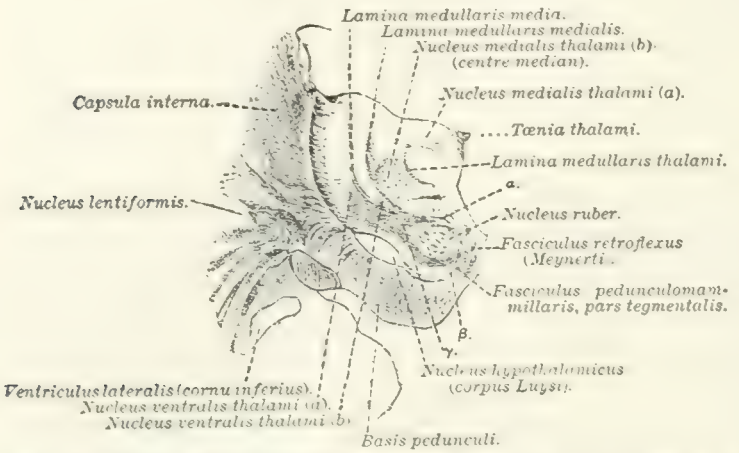

FIG. 945.—Frontal Section through a Normal Human Brain at the Level of the Lower End of the Nucleus Hypothalamicus. (After C. von Monakow, *Arch. f. Psychiat.*, Berlin, Bd. xxvii., 1895, Taf. iii., Fig. 20.) *α*, Dorsal white matter of nucleus ruber; *β*, ventral white matter of nucleus ruber; *γ*, lateral white matter of nucleus ruber. (From "The Nervous System and its Constituent Neurones," New York, 1900.)

The pars ventralis thalami is represented here by a narrow zone lying ventrally and laterally of the nuclei just enumerated. It includes the structures of the regio subthalamica and zona reticularis. It comprises the Feld H_2 of Forel, the corpus Luysi (often termed the corpus hypothalamicum of Luys) and at least the ventral part of the zona reticularis. These regions receive collaterals of the descending tracts of the basis pedunculi and also short tracts from the overlying nuclei of the pars dorsalis thalami (especially the medial nuclei) for intrinsic thalamic reflexes. They discharge directly backward into the tegmentum and do not send important tracts forward into the cerebral cortex.

The lateral and ventral nuclei of the pars dorsalis thalami and the metathalamus are concerned chiefly with cortical connections and give rise to the somatic sensory cortical radiations. They also receive return cortico-thalamic tracts from the cortex. The medial group of nuclei (stratum griseum centrale, nucleus medialis and nucleus anterior or dorsalis) are, as already stated, chiefly concerned with the intrinsic thalamic reflexes. They are all intimately connected with the olfacto-visceral centers of the hypothalamus, the nucleus anterior in particular receiving the tractus mammillo-thalamicus (Vicq d'Azyri) from the mammillary body, these fibers arising as collaterals of those of the tractus mammillopeduncularis. The evidence regarding cortical connections of these medial nuclei is conflicting. They unquestionably send ascending fibers into the cerebral hemisphere, but these fibers are said by Sachs to reach no farther forward than the nucleus caudatus of the corpus striatum. They are also connected with the basal olfactory area about the anterior perforated space through the pedunculus thalami medialis.

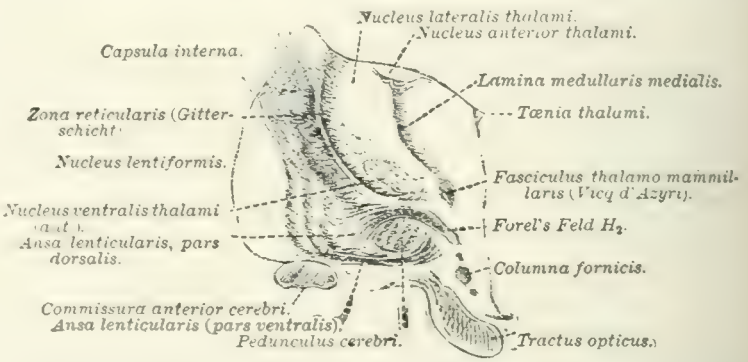

FIG. 946.—Frontal Section through a Normal Human Brain at the Level of the Ansa Lenticularis (anterior to the nucleus hypothalamicus). (After C. von Monakow, *Arch. f. Psychiat.*, Berlin, Bd. xxvii., 1895, Taf. iii., Fig. 28.) (From "The Nervous System and Its Constituent Neurones," New York, 1900.)

Some of the connections of the diencephalon are illustrated by the following diagrams, Figs. 948, 949, 950, 973, 989.

The Ophthalmencephalon.—This name may be applied to those portions of the brain which are concerned with the visual functions, a companion system to the rhinencephalon. It includes the retina, the optic part of the thalamus (pulvinar and lateral geniculate body), the colliculus superior (optic lobes of lower vertebrates) and the optic centers in the occipital lobe of the cerebral cortex.

We have already considered the mode of formation of the retina, as a lateral evagination from the wall of the diencephalic portion of the neural tube in

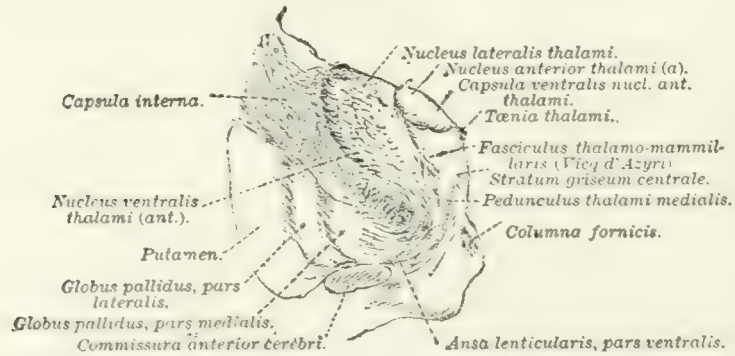

FIG. 947.—Frontal Section through a Normal Human Brain at Level of Anterior Part of Thalamus. (After C. von Monakow, *Arch. f. Psychiat.*, Berlin, Bd. xxvii., 1895, Taf. iv., Fig. 33.) (From "The Nervous System and Its Constituent Neurones," New York, 1900.)

early embryological stages (Figs. 898, 899). It is as truly a part of the brain as is the cerebral hemisphere, and the so-called optic nerve is an association tract of centers are in the strict sense of the word cortical dependencies, for they attain to only very insignificant proportions in forms with rudimentary cortex

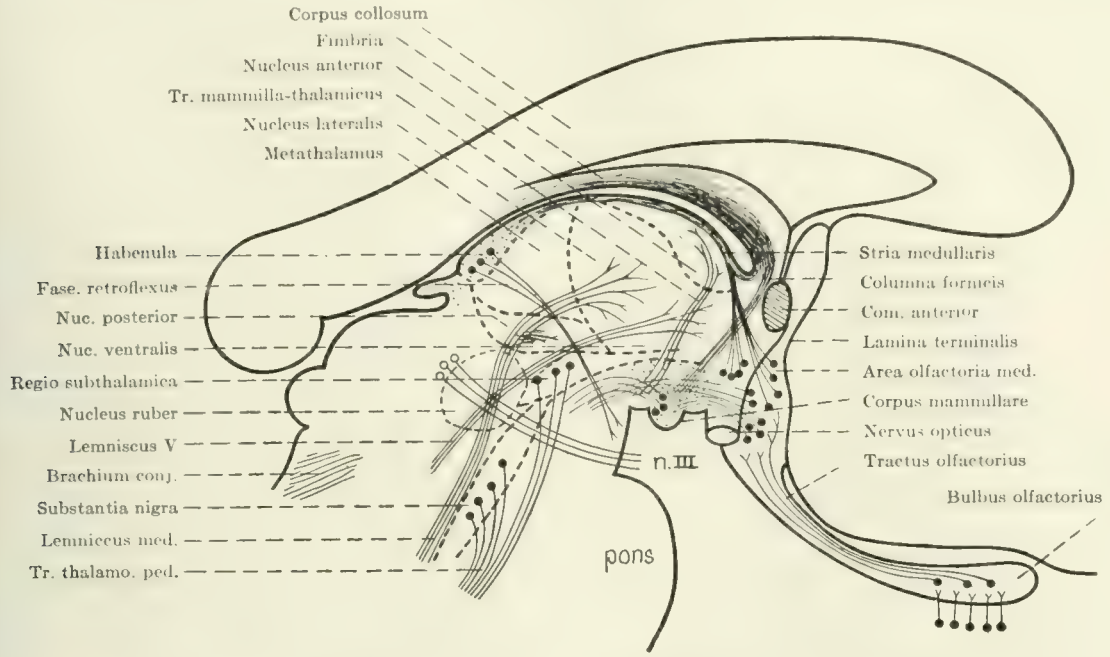

Fig. 948.—Scheme of the Nuclei of the Thalamus seen as Projected upon a Parasagittal Plane. The epithalamus and hypothalamus are stippled.

the same order as the lemniscus. Like the lemniscus, it decussates completely in the optic chiasma in lower vertebrates before terminating in the thalamus and midbrain. It is only in animals with an overlapping of the fields of vision of the two eyes, or stereoscopic vision, that the decussation of the optic tracts in the chiasma is incomplete.

In lower vertebrates the midbrain connections of the optic tracts are much more important than the thalamic, the latter connection being made by collaterals merely of the optic tract fibers as they cross the lateral face of the thalamus. The optic connections in the roof of the colliculus superior (tectum opticum) are practically all on the reflex plane in all animals. Here in the tectum the optic impulses are brought into relation with general sensory and auditory impulses coming in by way of the medial and lateral lemniscus respectively. In fishes and amphibians nearly all of the lemniscus fibers, as well as the optic fibers, end in the midbrain, very few passing on without interruption into the thalamus. From the tectum mesencephali important reflex connections are effected with the underlying motor centers of the tegmentum and with lower motor centers by important tecto-bulbar and tecto-spinal tracts. The midbrain connections of the optic system in the human brain are of this type, only the simpler visual reflexes being localized here; see Fig. 950.

The thalamic connections of the optic tracts in the lowest vertebrates are very insignificant, collaterals of this system being given off to terminate in the unspecialized association tissues of the pars dorsalis thalami. But in all forms with a differentiated cerebral cortex these thalamic optic connections assume greater importance, a special part of the pars dorsalis being set apart for their use. Thus arises the lateral geniculate body, and in higher mammals this is supplemented by the pulvinar. These

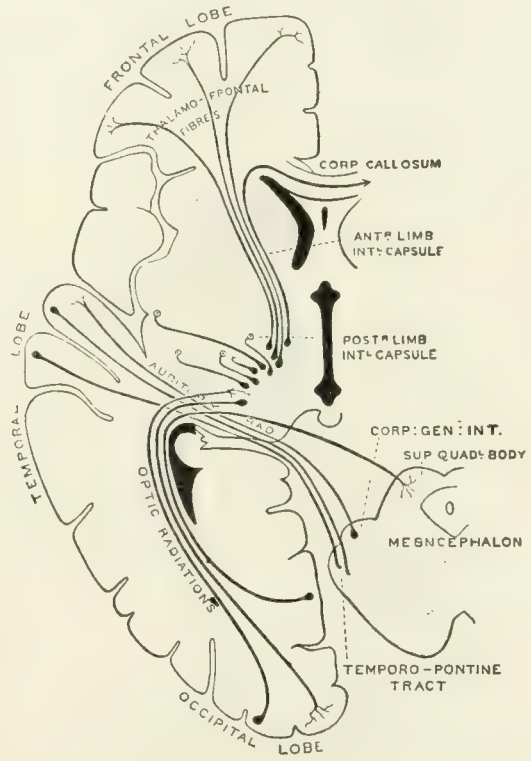

Fig. 949.—Scheme of the Thalamo-cortical Connections, Founded on the Observations of Flechsig, and Ferrier and Turner. (From Cunningham's Anatomy.)

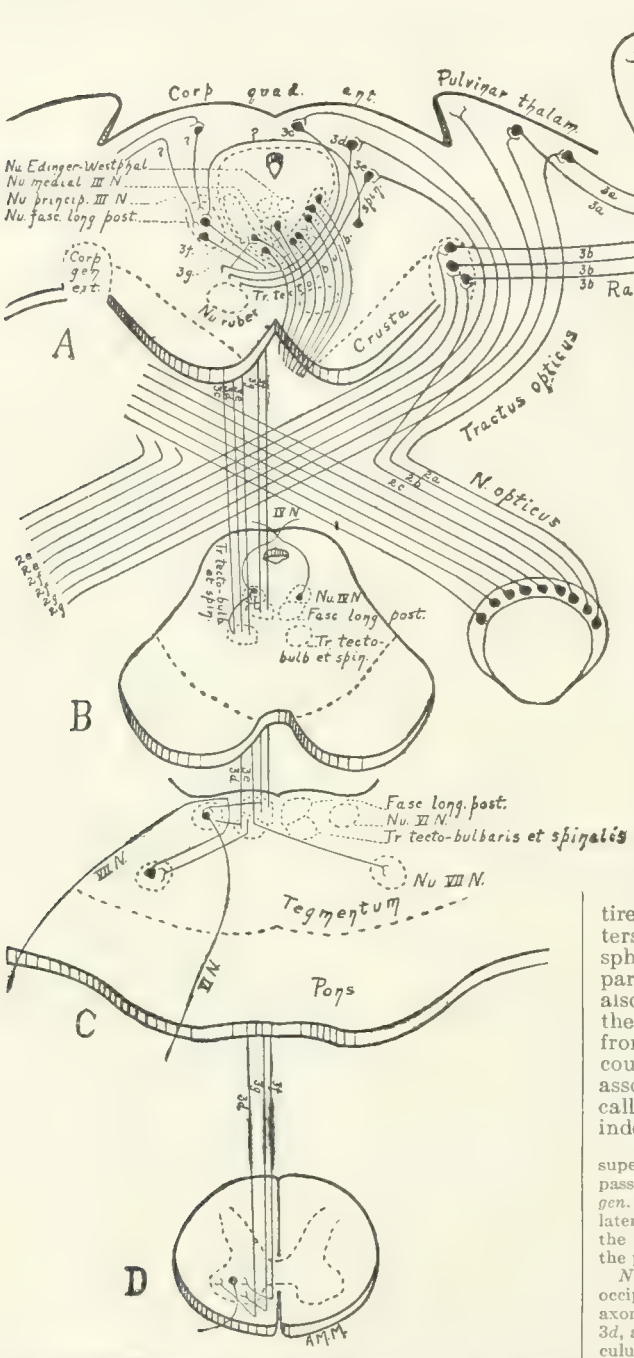

FIG. 950.—Diagram of the Optic Connections of the Brain (ophthalmencephalon). *A*, Section at the level of the II and III. cerebral nerves; *B*, at the level of the IV. nerve; *C*, at the level of the VI. and VII. nerves; *D*, spinal cord. (Designed by O. S. Strong; from Bailey's Histology.)

Neurone No. 1.—The rods and cones of the retina, which serve as the sensory receptive cells, and the bipolar cells of the retina, which constitute the neurones of the first order, are not indicated on the diagram.

Neurone No. 2.—The neurones of the second order are the cells of the ganglionic layer of the retina, whose axones make up the larger part of the fibers of the optic "nerve" and tract. Efferent fibers also pass from the brain to the retina, which are not indicated on the diagram. 2*a*, Axones of ganglion cells in the temporal part of the retina passing to the pulvinar of the same side; 2*b*, axones of the ganglion cells of the retina passing to the colliculus superior of the same side; 2*c*, axones of ganglion cells of the retina passing to the lateral geniculate body of the same side (*Corp. gen. ext.*); 2*e*, axones of ganglion cells of the retina passing to the lateral geniculate body of the opposite side; 2*f*, similar axones to the colliculus superior of the opposite side; 2*g*, similar axones to the pulvinar of the opposite side.

Neurone No. 3.—3*a*, Axones of cells in pulvinar to cortex of occipital lobe of cerebrum (this connection is disputed); 3*b*, axones of cells in lateral geniculate body to occipital cortex; 3*c*, 3*d*, and 3*e*, axones of cells in middle layer of tectum (roof) of colliculus superior decussate ventral to the fasciculus longitudinalis medialis (dorsal tegmental decussation, or decussation of Meynert) and form the tractus tecto-bulbaris et spinalis (*Tr. tecto-bulb. et spin.*) to bulb (medulla oblongata) and ventral column of spinal cord, innervating by collaterals and terminals, directly or indirectly chiefly the nuclei of III., IV., VI. and VII. cerebral nerves and motor nuclei of spinal nerves. 3*f* and 3*g*, (possibly another neurone intercalated between these and optic terminals), axones of cells in nucleus of fasciculus longitudinalis medialis (*Nuc. fasc. long. post.*), or nucleus of Darkschewitsch, form part of the fasciculus longitudinalis medialis (*Fasc. long. post.*) and descend on the same side to the ventral column of the spinal cord next to the ventral medial fissure, innervating nuclei of III., IV. and VI. cerebral nerves and motor nuclei of spinal nerves.

Neurone No. 4.—Axones of the cells in the above-mentioned motor nuclei, transmitting impulses directly to the peripheral muscles.

cerebri, but increase *pari passu* with the elaboration of the visual cortex.

Various authors have described other optic tracts leaving the optic chiasma to effect connections farther ventrally than either of the dorsal regions referred to above. These connections pass directly into the ventral motor lamina of the brain stem and are supposed to serve the most simple and rapid optic reflexes. They have been described as going to the subthalamic region, the hypothalamus and the tegmentum. But their study is very difficult, for a complete analysis of the optic chiasma and the associated postoptic commissural fibers (which have nothing to do with the visual apparatus directly) has never been made, and the whole question is one for further research.

The more important optic connections are indicated diagrammatically in Fig. 950, where the sharp contrast between the more primitive mesencephalic connections of the direct reflex type and the thalamic connections with relations to the cerebral cortex, is clearly manifest.

The Telencephalon.—The cerebral hemispheres begin as lateral outgrowths from the rostral end of the neural tube. These, as we saw on a previous page, finally involve the whole of the lateral walls in this region except the part immediately adjacent to the optic chiasma and preoptic recess (preoptic nucleus, or ganglion opticum basale). The development of lower brains shows that the initial cerebral evagination was called forth by the olfactory apparatus, and in fishes and amphibians, even in the adult, the olfactory function dominates practically the entire hemisphere. Fibers from the non-olfactory centers of the brain stem ascend to enter the hemispheres, however, in fishes, these fibers ending in part in various olfactory correlation centers and also in a special part of the hemisphere called the "somatic area," which is nearly or quite free from direct olfactory connections. When in the course of further evolution these non-olfactory association fibers become sufficiently developed to call for associations *inter se* within the hemispheres independently of the olfactory centers, their somatic

association centers become separated from the olfactory centers. Thus arise the corpus striatum and neopallium. Those parts of the brain which remain under the dominant influence of the olfactory function in the aggregate are termed the rhinencephalon.

The adult hemisphere may, therefore, be divided into the rhinencephalon, or olfactory division, and the non-olfactory division. The former, as here defined, includes the primary olfactory or receptive center in the olfactory bulb, basal olfactory correlation centers in the anterior perforated space, septum, etc., and the olfactory cortex, including the hippocampus and uncus (pyriform lobe of lower mammals). The olfactory cortex (sometimes termed archipallium) is devoted chiefly to the correlation of olfactory with gustatory and visceral impressions. The non-olfactory division includes the basal corpus striatum complex and the non-olfactory cerebral cortex or neopallium. This division is sometimes called the somatic division of the hemisphere and the neopallium the somatic cortex.

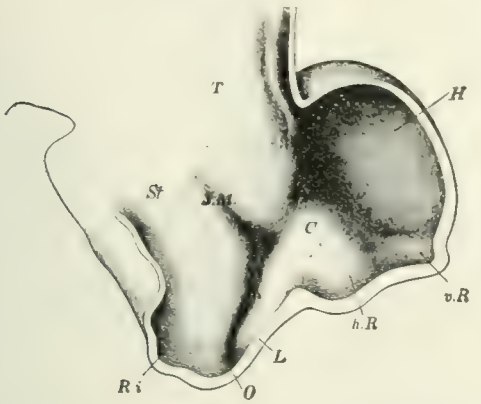

Fig. 951.—View of the Inside of the Lateral Wall of the Anterior Part of the Forebrain of a Human Embryo of about Four and One-Half Weeks. *C*, Corpus striatum; *H*, pallium; *h.R.* posterior olfactory lobe; *L*, lamina terminalis; *O*, recessus preopticus; *R.i.*, recessus infundibuli, His (recessus postopticus, Johnston); *S.M.*, sulcus hypothalamicus (sulcus Monroi, His); *St.*, hypothalamus; *T.*, thalamus; *v.R.*, anterior olfactory lobe. (After His, from Bailey and Miller's Embryology.)

The entire hemisphere is often subdivided in accordance with a different principle into a basal or stem portion and a dorsal portion, the cortex or pallium. The basal portion includes the centers for reflex and instinctive functions in the corpus striatum and lower olfactory centers; the cortical portion includes the neopallium and archipallium, devoted to higher correlations and conscious reactions.

The form of the hemispheric evagination in an embryo of four and one-half weeks (as computed by His; probably in reality somewhat older) is seen in Fig. 951 (cf. Fig. 886). The pallium is clearly separate from the stem portion of the telencephalon, the latter at this age being only partially evaginated into the hemisphere. An embryo about one week older is seen in Fig. 896. In both of these figures the basal or subcortical portion of the hemisphere consists of a lateral corpus striatum and a medial olfactory area, comprising an anterior olfactory lobe, most of which becomes the olfactory bulb, and a posterior olfactory lobe (the Trapezfeld of His), which later becomes the tuberculum olfactorium and other parts of the anterior perforated space, the septum and the precommisural body, all of which belong in the rhinencephalon. In later stages the rhinencephalon becomes more clearly separated from the somatic area of the hemisphere, medially by a fissura prima (Fig. 952) and laterally by an external rhinal fissure which lies immediately external to the gyrus olfactorius lateralis of Fig 953.

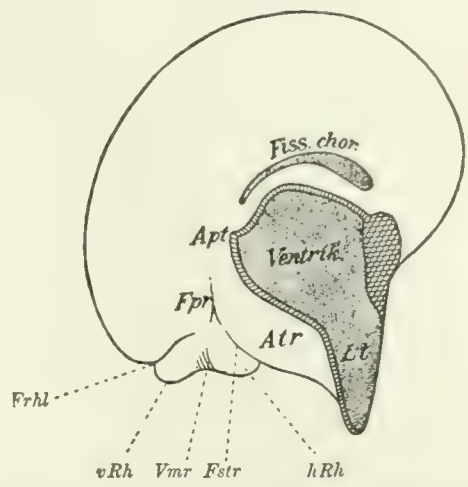

Fig. 952.—Diagram of a Graphic Reconstruction of the Medial Wall of the Cerebral Hemisphere of a Human Embryo of Sixteen Millimeters (about six weeks). Cavities are dotted, cut surfaces are lined. *Apt*, Angulus prethalamus; *Atr.*, preterminal area; *Fpr.*, anterior arcuate fissure (fissura prima); *Frhl*, mesial termination of lateral rhinal fissure; *hRh.*, posterior olfactory lobe (tuberculum olfactorium + substantia perforata anterior); *Lt*, lamina terminalis (lined); *Vmr.*, depression between the two olfactory lobes; *vRh.*, anterior olfactory lobe (bulbus olfactorius + tractus olfactorius + trigonum olfactorium). (After His and Ziehen, from Bailey and Miller's Embryology.)

Plexuses.—The membranous roof of the diencephalon is extended downward and forward to join the lamina terminalis, thus forming the roof of the foramen of Monro (Figs. 891, 954). This part of the roof belongs within the telencephalon and is termed by Johnston the lamina supraneuroporica. The diencephalic part of this roof plate becomes vascular and, together with the adjacent pia mater, is convoluted to form the chorioid plexus of the third ventricle.

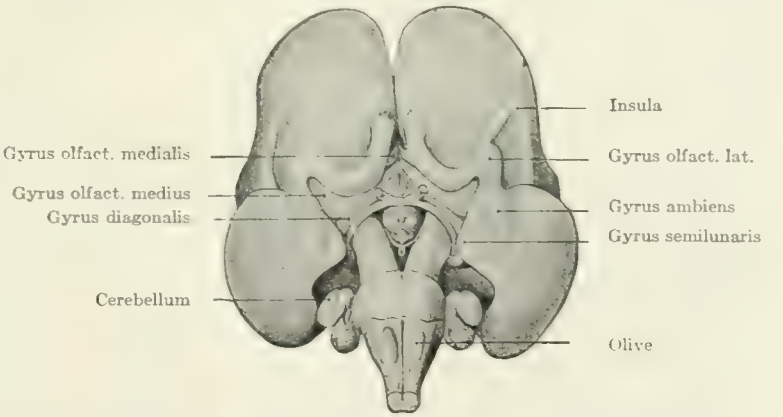

Fig. 953.—Ventral View of the Brain of a Human Fetus at the Beginning of the Fourth Month. (After Kollmann, from Bailey and Miller's Embryology.)

The medial wall of the posterior part of the embry-

FIG. 954.—Dorsal View of a Model of a Brain of a 13.6-Millimeter Human Embryo (sixth week). The dorsal part of the pall. an. on each side has been removed: *cf.* Fig. 891. (After His, from Bailey and Miller's Embryology.)

onic hemisphere which covers the thalamus and is connected with the lamina supraneuroporica is membranous. In the adult this becomes a portion of the medial wall of the inferior horn of the lateral ventricle, bordered by the hippocampus and fimbria. This membranous portion is folded inward through the chorioid fissure to form the lateral plexus of the hemisphere (Figs. 952, 954, 955, 967, 968, 971, 977), and in the adult a part of it becomes secondarily attached to the thalamus, forming the lamina affixa. The

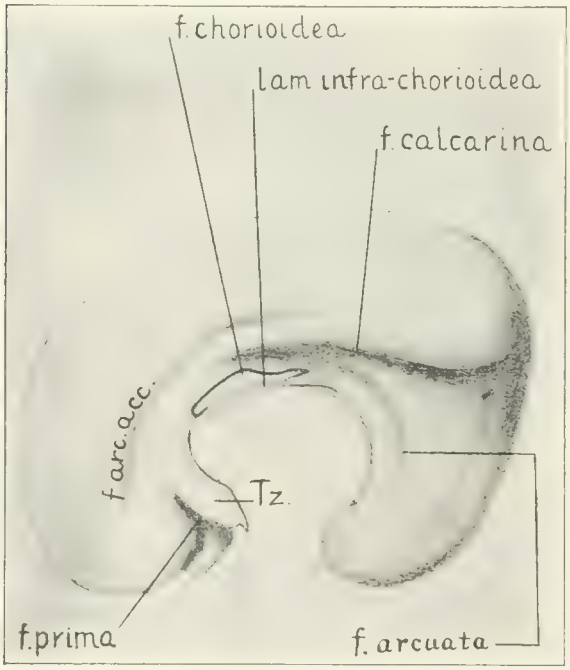

FIG. 955.—Medial Surface of the Hemisphere of a Human Fetus of about Three Months (5.3 centimeters long). *f. arc. acc.*, Fissura arcuata accessoria; *Tz.*, trapezfeld or precommissural body. (After His.)

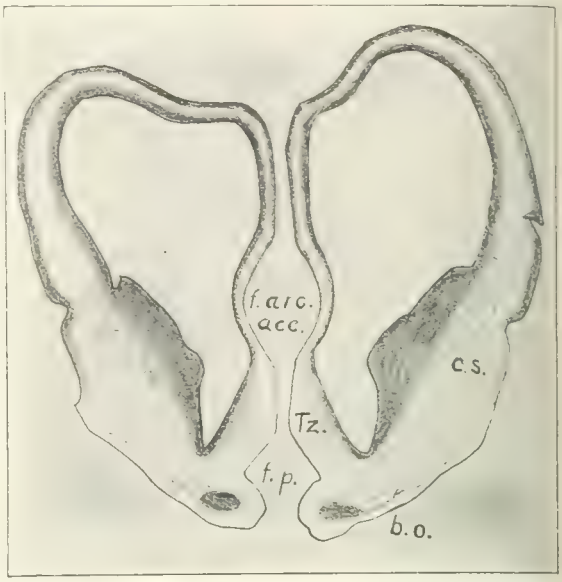

FIG. 956.—Transverse Section through the Cerebral Hemispheres in Front of the Lamina Terminalis of Human Fetus of about Three Months (5.6 centimeters long). *b.o.*, Bulbus olfactorius; *c.s.*, corpus striatum; *f. arc. acc.*, fissura arcuata accessoria; *f.p.*, fissure prima; *Tz.*, trapezfeld or precommissural body. (After His.)

line of attachment of the chorioid plexus to the lamina affixa is termed the tænia chorioidea, while the line of attachment of this membrane on the other side of the chorioid fissure to the hippocampus is known as the tænia fornicis. The latter is bounded by a strong band of fibers, the fimbria. This contains fibers of the commissura hippocampi, connecting the hippocampus of one hemisphere with that of

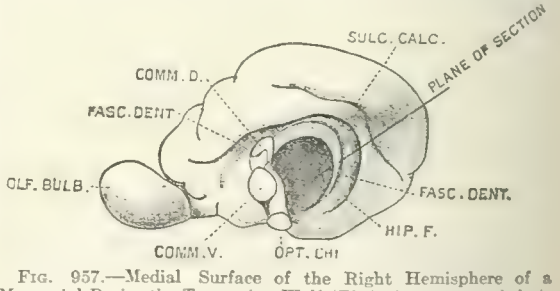

FIG. 957.—Medial Surface of the Right Hemisphere of a Marsupial Brain, the Tasmanian Wolf (*Thylacinus cynocephalus*), Illustrating the Course of the Hippocampus (*fasc. dent.*) from the Region of the Septum Medially along the Border of the Cortex and Around the Posterior Pole to the Pyriform Lobe on the Ventro-Lateral Surface. The corpus callosum is absent. × ¾ *comm. d.*, Commissura dorsalis (hippocampi); *comm. v.*, commissura ventralis (anterior); *fasc. dent.*, fascia dentata of the hippocampus; *hip. f.*, hippocampal fissure; *olf. bulb*, olfactory bulb. *opt. chi.*, optic chiasma; *sulc, calc.*, sulcus calcarinus. (After Elliot Smith.)

the other, and ascending and descending fibers of the fornix system between the hippocampus and various subcortical regions. Compare the discussion of the lateral plexuses under the heading *Meninges* at the end of this article.

The Rhinencephalon.—The basal part of the rhinen-

cephalon consists of a gyrus olfactorius medialis (which is continuous dorsally with the septum

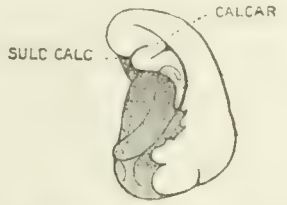

Fig. 958.—An Oblique Section through the Hemisphere of the Tasmanian Wolf in the Plane Indicated on Fig. 957, Illustrating the Relations of the Hippocampal Fissure and Hippocampus. (After Elliot Smith.)

pellucidum), a gyrus olfactorius lateralis and an intervening series of centers in the anterior perforated

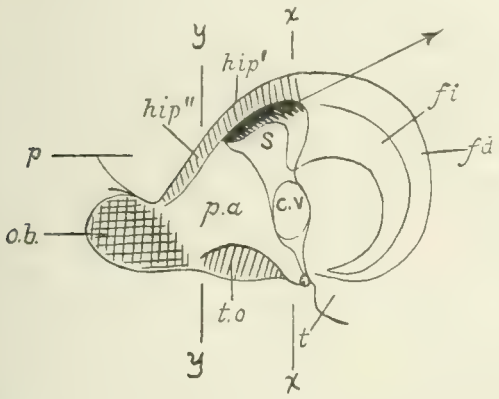

Fig. 959.—Scheme to Show the Arrangement of the Hippocampus in the Medial Wall of the Hemisphere of a Marsupial Brain. *c.v.*, Commissura ventralis (anterior ; *fd*, postcommissural hippocampus; *fi.*, fimbria; *hip'*., supracommissural hippocampus; *hip''*., precommissural hippocampus; *o.b.*, olfactory bulb; *p.*, neopallium; *p.a.*, precommissural body; *s.*, commissure bed; *t.*, temporal pole of the cerebral hemisphere; *t.o.*, tuberculum olfactorium; *x–x*, plane of section of Fig. 961; *y–y*, plane of section of Fig. 962. (After Elliot Smith.)

space (Fig. 953). The corpus striatum, which in earlier stages occupies the ventrolateral wall of the hemisphere, at this age has withdrawn from the surface (Fig. 956), so that the entire margin of the dorsal, or cortical, part of the hemisphere rests upon the basal olfactory area.

This marginal part of the cortex becomes the archipallium. The gyrus olfactorius lateralis extends directly backward into a pallial eminence (larger in lower mammals), the lobus pyriformis, which in the adult becomes the gyrus ambiens and the gyrus semilunaris of the uncus. From these centers the hippocampus is continued dorsally around the posterior margin of the embryonic hemisphere (buried within the substance of the temporal lobe in the adult) to the medial surface. On the medial surface the hippocampus is separated from the neopallium by the fissura arcuata (Fig. 955), the posterior part of which in the adult becomes the fissura hippocampi.

In some lower mammals, where the rhinencephalon is more highly developed than in man and where the corpus callosum is absent, this fissure is in the adult continued forward into the position of the embryonic fissura prima, and the hippocampus extends forward into contact with the olfactory nuclei of the septum. Comparison of Fig. 957 with Fig. 955 shows that in the adult marsupial (opossum, kangaroo, etc.), the hippocampal fissure is the equivalent of the fissura arcuata and the fissura prima and that in the marsupial the hippocampus (fascia dentata) is con-

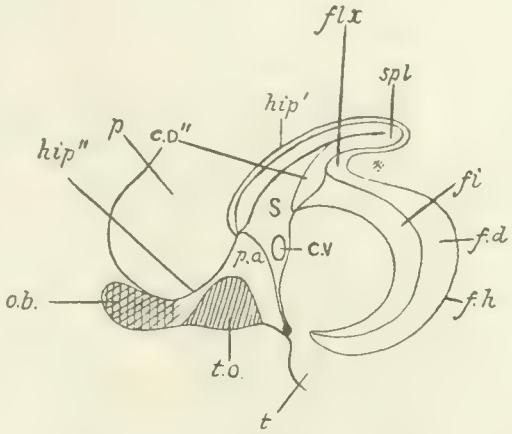

Fig. 960.—Scheme similar to Fig. 959 of the Corresponding Region of a more Highly Developed Cerebrum, Such as that of the Bat, *Pteropus*. Reference letters as before, and in addition: *C.D.''*., commissura hippocampi; *f.h.*, fissura hippocampi; *flx.*, the subsplenial hippocampal flexure; *spl.*, splenium corporis callosi; * gyrus subsplenialis (Levi) or gyrus Andreæ Retzii. (After Elliot Smith).

tinuous from the septum in front to the pyriform lobe around the posterolateral border of the cortex.

In the marsupials the anterior commissure (Fig. 957, *comm. v.*) is very large and the hippocampal commissure (*comm. d.*) is also well developed, but there is no corpus callosum. The relations of the hippocampus in a marsupial brain are shown schematically in Fig. 959, where the hippocampus is seen to be composed of a postcommissural portion (*fd.*), a supracommissural portion (*hip.'*) and a precommissural portion (*hipp.''*). The hippocampal commis-

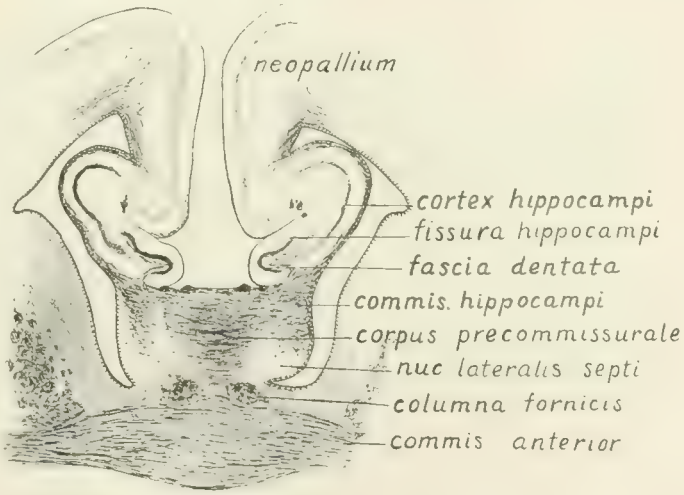

Fig. 961.—Transverse Section through a Portion of the Cerebral Hemisphere of the Opossum, Didelphys virginiana, Including the Anterior Commissure, the Hippocampal Commissure and the Supracommissural Hippocampus. Drawn from a preparation made by Dr. G. E. Coghill, Weigert method. × 7. The section passes in approximately the plane marked *x–x* on Fig. 959.

sure (marked by the arrow) is bent backward in the form of a U. In higher mammals corpus callosum fibers appear in the dorsal commissure in the position of the deeply shaded area at the end of the arrow. With the increase in number of the callosal fibers this horizontal limb of the dorsal commissure is extended both forward and backward, the direction of the backward growth being indicated by the arrow in the figure. The result is the form shown in Fig. 960, which illustrates the brain of one of the larger bats, Pteropus. The supracommissural portion of the hippocampus now suffers reduction.

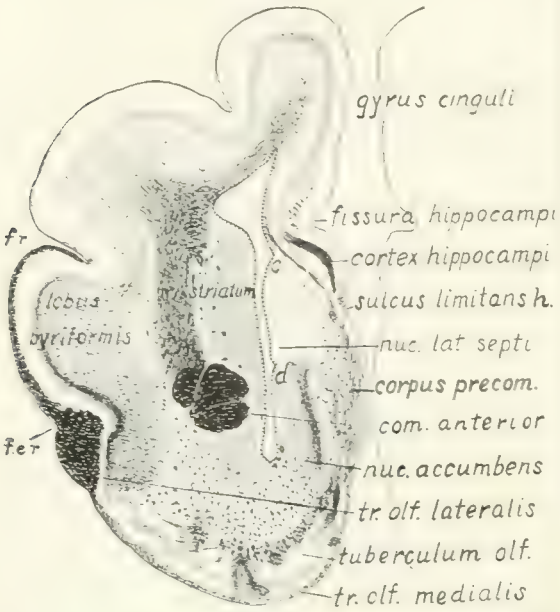

Fig. 962.—A Similar Section from the Same Series Farther Forward, Approximately in the Plane marked *x–x* on Fig. 959. The fissura hippocampi is much shallower and there is no differentiation between the cortex hippocampi and the fascia dentata. The hippocampus is marked off from the underlying septum by a limiting sulcus (sulcus limitians hippocampi), whose inner or ventricular location is marked by a slight groove at *c*. A similar ependymal groove, *d*, separates the septum from the nucleus accumbens septi, which belongs to the corpus striatum complex. The tuberculum olfactorium is separated from the overlying precommissural body and septum by a slight sulcus, not named on the figure. The section passes through the rostral end of the lobus pyriformis, here perhaps better termed nucleus olfactorius lateralis, for its entire surface is covered by fibers of the lateral olfactory tract. It is limited by a fissura rhinalis (ectorhinalis, *f.r.*) above and a fissura endorhinalis (*f.e.r.*) below.

A transverse section through the brain of the Virginia opossum (Fig. 961) in the position marked *x–x* on Fig. 959 illustrates the relations of the anterior commissure and hippocampal commissure to the supracommissural hippocampus. In the absence of the corpus callosum, this part of the hippocampus exhibits essentially the same structure as the postcommissural part. A similar section through the brain of the opossum (Fig. 962), taken approximately in the plane *y–y* indicated on Fig. 959, shows the fissura hippocampi and the reduced, but still evident, hippocampal cortex extending forward over the septum and precommissural body into contact with the olfactory bulb.

Turning now to the true mammals (Eutheria), in which a corpus callosum is present and interpolated between the hippocampus and the septum (cf. Figs. 959 and 960), the supracommissural part of the hippocampus suffers very great reduction. It is much better developed in the lower members of this group, like rodents, bats and insectivorous mammals; but even in man a vestige of it is preserved in the indusium griseum of the corpus callosum.

An examination of the medial surface of the cerebral hemisphere of the rat (Fig. 963) shows fundamentally the same relations as in marsupials. The supracommissural portion of the hippocampus (gyrus supracallosus) is small but evident, the hippocampus as a whole being arranged as in Fig. 957 save for the changes of size and position necessitated by the development of the corpus callosum.

A section through the brain of the rat taken parallel to the sagittal plane and close to the midline (Fig. 964) shows the dorsal end of the postcommissural part of the hippocampus (tuberculum of the fascia dentata) and its extension through the gyrus subsplenialis and fasciola cinerea around the splenium of the corpus callosum into continuity with the greatly reduced supracallosal part of the hippocampus

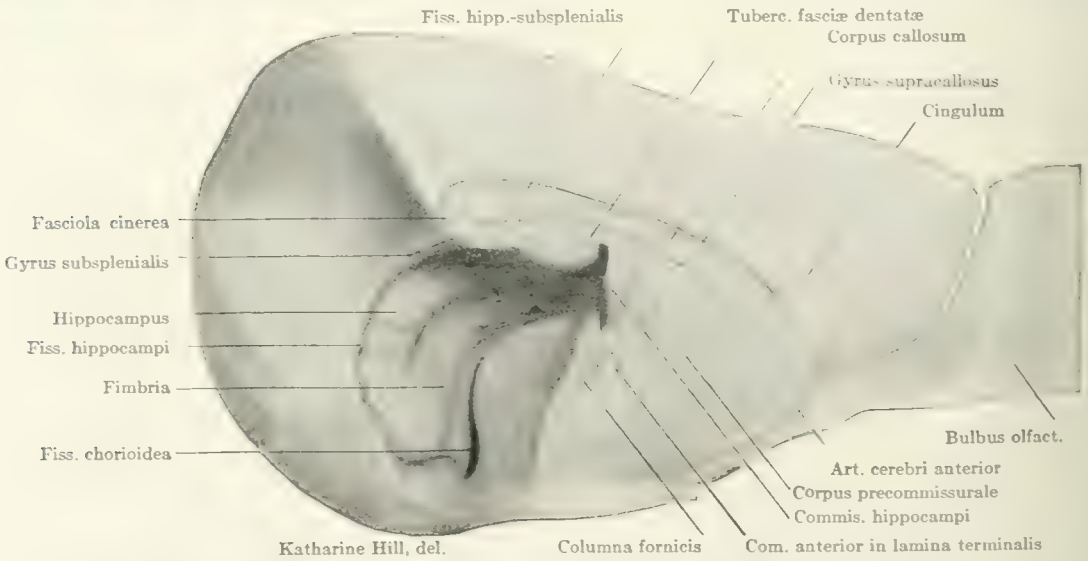

Fig. 963.—Medial Surface of the Left Hemisphere of the Brain of a White Rat. The thalamus has been cut away behind the anterior commissure to expose the full extent of the hippocampus and the medial border of the pyriform lobe. × 6.

(cf. Fig. 960). The latter enlarges slightly at the rostral end (gyrus supracallosus), and still farther forward the precommissural part drops down into contact with the septum and precommissural body and in considerably enlarged form extends forward to the olfactory bulb. Fig. 965 illustrates the greatly reduced form of the supracommissural hippocampus (gyrus supracallosus), as seen in cross-section taken through the septum (precommissural body) between the anterior commissure and the rostral end of the corpus callosum. Fig. 966 is a similar section taken farther forward, in front of the corpus callosum, illustrating the enlarged precommissural hippocampus

callosum is accompanied by a reduction of the supracommissural part of the hippocampus, until in the adult the latter is represented in very vestigeal form in the gray indusium of the callosum (Fig. 970). Here the postcommissural part of the hippocampus has remained unmodified and is folded into the lateral ventricle to form the cornu Ammonis.

The arcuate fissure of the embryo is a total fold of the medial wall of the pallium. The adult hippocampus is constituted by the walls of the same fissure, here called fissura hippocampi, with the further complication that cells have multiplied at the free margin of the hippocampus where it is bor-

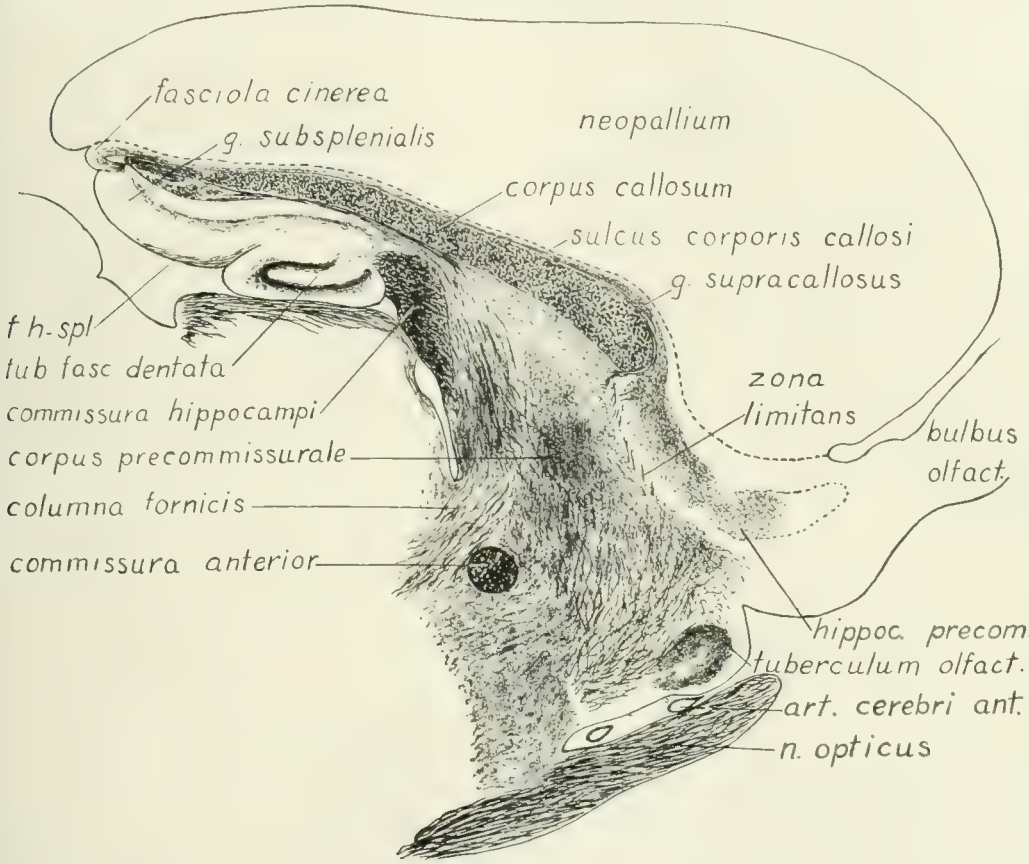

FIG. 964.—A Parasagittal Section taken about 0.5 Millimeters from the Medial Plane of the Brain of a White Rat. The dorsal end of the fascia dentata and the full extent of the hippocampus dorsalis are shown in this figure, except the extreme rostral end of the precommissural hippocampus, which extends farther forward out of the plane of the section, as indicated by the dotted outline. The full extent of the sulcus corporis callosi and its extension forward above the precommissural hippocampus (*cf.*, Fig. 966) is projected upon the figure from adjacent sections, as indicated by the broken line. This sulcus is morphologically an extension of the fissura hippocampi. *f.h.–spl.*, Fasciculus hippocampo-susplenialis, from the stratum lacunosum of the hippocampus to the gyrus subsplenialis and neopallium farther caudad; *hippoc. precom.*, precommissural hippocampus. (From a preparation stained by the method of Weigert-Pal and carmine made by Dr. Elizabeth H. Dunn. × 15.)

in relations which are very similar to those of marsupials (cf. Fig. 962).

Thus, in the rat, as in the marsupials, the entire margin of the pallium is bordered by the rhinencephalon—on the medial and posterior borders by hippocampus, and on the lateral border by the pyriform lobe and gyrus olfactorius lateralis. The rostral end of the latter is seen in Figs. 965 and 966 lying between the fissura rhinalis (ectorhinalis) and the fissura endorhinalis.

In the human brain of the fourth month the corpus callosum is beginning to develop, but the relations of the medial wall are still very similar to those of adult marsupials (Figs. 967, 968). In still later stages (Fig. 969) the increase in size of the corpus

dered by the fimbria to form the gyrus dentatus, or fascia dentata (Fig. 971). This has the form of a reverse fold of the cortex within the hippocampus and in the opposite direction, which is marked by a slight groove running parallel with the fissura hippocampi, the sulcus fimbrio-dentatus.

The hippocampus is bordered by the gyrus hippocampi, a superficial convolution which is covered with cortex of a type transitional between the cornu Ammonis and neopallium. Similarly the gyrus cinguli above the horizontal limb of the hippocampus in marsupials (Figs. 961, 962) is transitional between the supracommissural hippocampus and neopallium. In man its olfactory component is reduced. The gyrus hippocampi and gyrus cinguli are now com-

monly reckoned with the neopallium, though their participation in olfactory associations is recognized by their inclusion, together with the hippocampus and the basal part of the rhinencephalon, in the great limbic lobe of Broca.

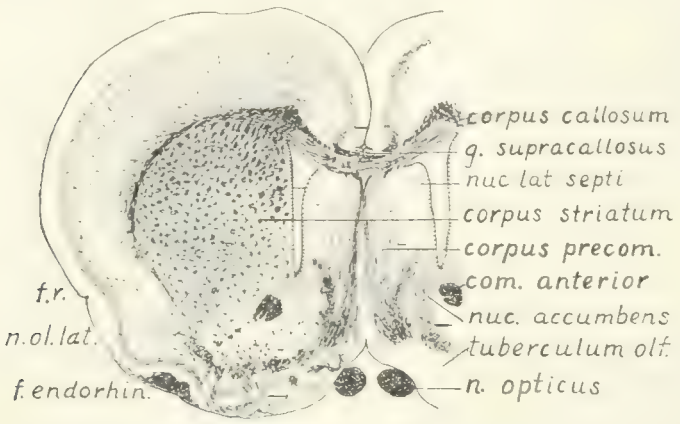

FIG. 965.—Transverse Section through the Brain of the White Rat, Passing through the Septum and Rostral End of the Corpus Callosum (*cf.*, Figs, 963, 964). The figure illustrates the greatly reduced supracommissural hippocampus (*g. supracallosus*), which is separated from the overlying neopallium by a slight sulcus corporis callosi (not named on the figure) which is the equivalent of the fissura hippocampi of marsupial brains (*cf.*, Fig. 961). The septum is greatly thickened to contain the nucleus lateralis septi (*nuc. lat. septi*) and precommissural body (*corpus precom.*). The tuberculum olfactorium occupies the ventral surface of the brain, being bounded laterally by a shallow fissura endorhinalis, under which is the lateral olfactory tract. The nucleus olfactorius lateralis (*n. ol. lat.*) is bounded below by the fissura endorhinalis and above by the fissura rhinalis, or ectorhinalis (*f.r.*). (Drawn from a Weigert-Pal and carmine preparation made by Dr. Elizabeth H. Dunn. × 7.)

Elliot Smith first clearly distinguished the hippocampus from the remainder of the cortex, which he termed neopallium. The hippocampus is sometimes termed the archipallium. The cortex of the pyriform lobe (uncus, etc.) is in an ambiguous position. By the usage here adopted the archipallium includes the hippocampus (cornu Ammonis, gyrus dentatus, indusium griseum, precommissural hippocampus, etc.) and the pyriform lobe. The remainder of the cortex is neopallium.

The human olfactory apparatus, when compared with that of most lower animals, is seen to be in a very reduced condition. Man, and primates in general, are classed as microsmatic animals, while most other mammals are macrosmatic (*e.g.* the opossum, rat, dog, etc.). From this it follows that the human rhinencephalon can be most easily understood by comparison with lower mammalian forms, in which this system is better developed and the non-olfactory part of the hemisphere is not only relatively but absolutely much smaller. The general plan of the rhinencephalon is, however, surprisingly constant throughout the vertebrate series, the neopallium being the most variable part of the brain.

The evolutionary history of the rhinencephalon may be briefly summarized as follows: In the lowest vertebrates the anterior end of the neural tube received the peripheral olfactory fibers and thus became differentiated as the primary olfactory area, or olfactory bulb, which was early enlarged so as to cause an evagination of the lateral wall on each side. Fibers of the second order (olfactory tracts) passed backward from the bulb to end in an association center of the second order, the area olfactoria. In the lowest existing vertebrates a part of this secondary area was also evaginated into the cerebral hemisphere. This is the condition found in the cyclostome fishes. Here the secondary area comprises a lateral region which is evaginated to form the greater part of the posterior lobe of the cerebral hemisphere and a medial region which remains unevaginated in the telencephalon medium adjacent to the lamina terminalis. In cyclostomes this medial region consists of two parts, (1) dorsal part, the primordium hippocampi, which in higher animals becomes the hippocampus, and (2) a ventral part which extends directly backward without interruption into the preoptic nucleus and hypothalamus. In higher forms the hippocampus is also evaginated into the cerebral hemisphere, as is also the rostral end of the ventral part (septum, tuberculum olfactorium, etc.).

These various parts of the secondary olfactory area at first were functionally much alike (cyclostomes); but in the course of further evolution this primordial simple secondary olfactory area becomes differentiated into many regions of very unlike nature. This specialization has taken place under the influence of fibers ascending from different lower non-olfactory centers in the diencephalon, etc., for various kinds of olfactory correlations. In general, fibers from the hypothalamus have reached the medial and dorsal parts of the olfactory area, while those from the thalamus have reached its lateral parts.

In the mammals, accordingly, we recognize in the area olfactoria the following parts: First, at the base of the olfactory bulb and extending more or less forward into the bulb is a *nucleus olfactorius anterior*, an unspecialized remnant of the primitive secondary nucleus which receives no important ascending tracts from the diencephalon. This is the region of the trigonum olfactorium of man. Second, we recognize an *area olfactoria lateralis*, which receives the lateral olfactory tract. It includes anteriorly the relatively unspecialized nucleus olfactorius lateralis (Fig. 965, *n. ol. lat.*), which in the human brain extends as far back as the limen insulæ (Figs. 938, 953, *Gyrus olfact. lat.*).

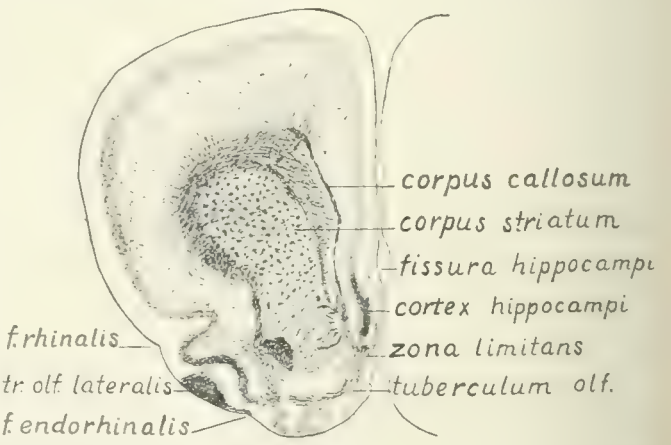

FIG. 966.—Transverse Section from the same Series as Fig. 965, Passing through the Rostral End of the Hemisphere in Front of the Corpus Callosum, to Illustrate the Relations of the Precommissural Hippocampus (*cf.*, Fig. 964). The forms of the cortex hippocampi and fissura hippocampi here are similar to those of marsupial brains in the corresponding region (Fig. 962). The fissura hippocampi is the forward continuation of the sulcus corporis callosi as seen in Fig. 964.

Farther back it is termed the lobus pyriformis in lower brains, a region which in the human brain is represented in the uncus region of the temporal lobe and the underlying nucleus amygdalæ. This entire area is reached by the lateral olfactory tract, and the amygdala (epistriatum of lower brains) is connected with the medial olfactory area by a strong fiber tract, the

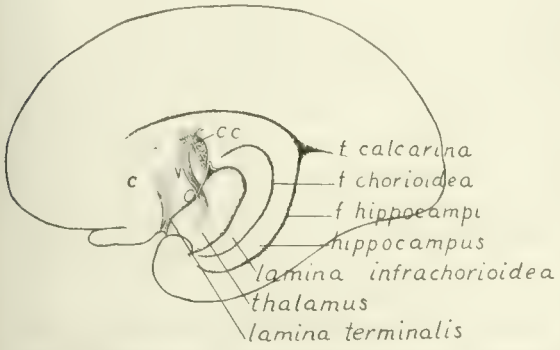

Fig. 967. Diagram of the Medial Surface of the Cerebral Hemisphere of a Human Fetus 8.3 Centimeters Long. *c.*, Area of contact of the two hemispheres; *c.c.*, rudiment of the corpus callosum; *v.*, area of fusion of the two hemispheres (precommissural body). (After His, slightly modified.)

stria terminalis, part of which crosses in the anterior commissure. The pyriform lobe develops in intimate relations with the underlying corpus striatum and probably with ascending projection fibers from the diencephalon. Third, the *area olfactoria medialis* comprises the region reached by the medial olfactory tract and by ascending fibers coming chiefly from the hypothalamus. It includes the nuclei of the septum, gyrus subcallosus, precommissural body and preoptic nucleus (ganglion opticum basale). Fourth, the *area olfactoria intermedia*, or *tuberculum olfactorium* lies between the lateral and medial areas and receives olfactory fibers from both lateral and medial tracts, but chiefly (in lower mammals, at least) the lateral. It is developed in intimate relation with the head of the caudate nucleus of the corpus striatum and, according to Edinger, receives ascending fibers of the sensory trigeminus system. In the human brain it occupies the greater part of the anterior perforated space, or locus perforatus anticus (Figs. 901, 938). Fifth, the *primordium hippocampi* in lower brains appears first as a dorsal secondary nucleus, which in mammals becomes the *hippocampus*. Its anterior end is, even in mammals (especially plainly in the lowest mammals; cf. Figs. 959, 964), in contact with the area olfactoria medialis. Posteriorly it curves around the posterior pole of the hemisphere into relation with the pyriform lobe of the area olfactoria lateralis (Fig. 963).

It will be possible to mention here only the more important fiber connections of the rhinencephalon. The olfactory fibers of the first order (fila olfactoria) arise from cells which lie in the Schneiderian membrane of the nasal cavity and terminate in tufted endings

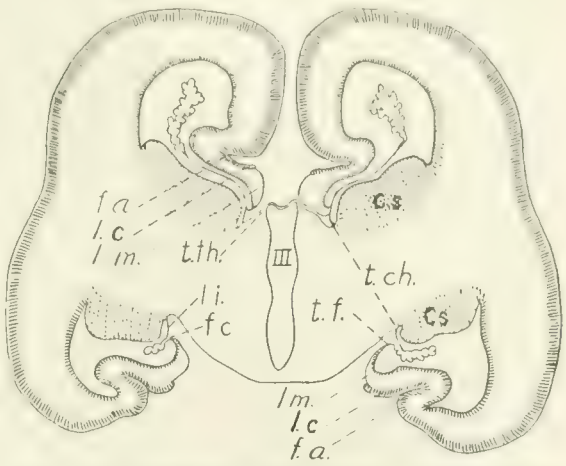

Fig. 968.—Cross Section through the Brain of a Human Fetus 8.3 Centimeters Long. *c.s.*, Corpus striatum; *f.a.*, fissura arcuata; *f.c.*, fissura chorioidea; *III.* third ventricle; *l.c.*, limbus corticalis; *l.i.*, lamina infrachorioidea; *l.m.*, limbus medullaris; *t. ch.*, tænia chorioidea; *t.f.*, tænia fornicis; *t. th.*, tænia thalami. (After His.)

among the dendrites of the mitral cells of the olfactory bulb; these masses of interlacing unmedullated fibers which constitute the synapse are termed olfactory glomeruli (Fig. 972). Below the mitral cells is a thick layer of very minute granule cells which resemble somewhat the cerebellar granules and which, like the latter, probably serve to reinforce the relatively weak impulses discharged by the mitral cells. The formatio bulbaris, or characteristic structure of the olfactory bulb, consists, accordingly, of four well-

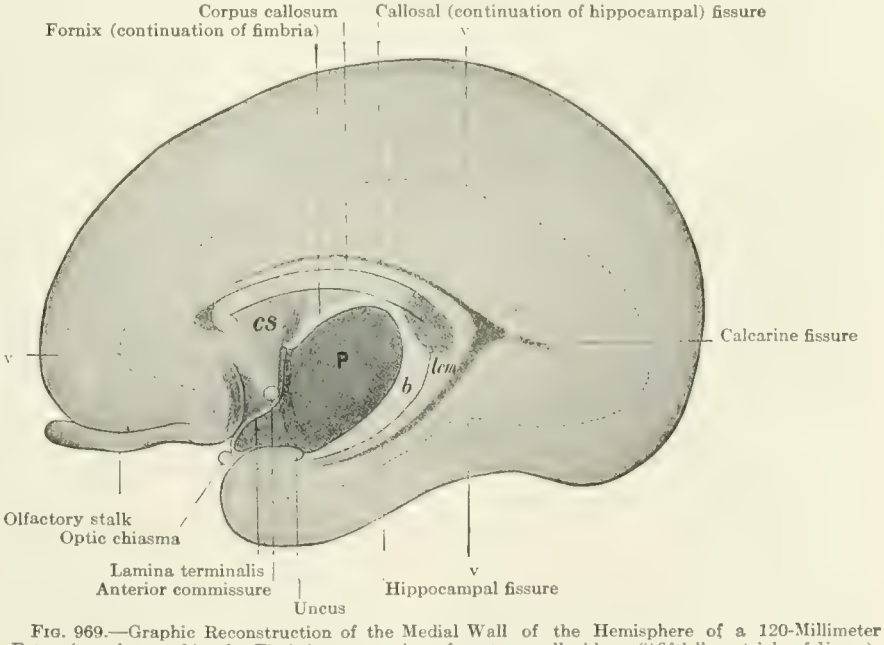

Fig. 969.—Graphic Reconstruction of the Medial Wall of the Hemisphere of a 120-Millimeter Fetus (fourth month). *b.*, Fimbria; *cs.*, cavity of septum pellucidum ("fifth" ventricle of Verga); *lcm.*, limbus corticalis (gyrus dentatus); *P.*, cerebral peduncle; *v.*, outline of cavity of hemisphere (lateral ventricle). (After His, from Quain's Anatomy.)

defined layers which are concentrically arranged. Externally is a layer of olfactory nerve fibers, then the glomerular layer, the layer of mitral cells and finally

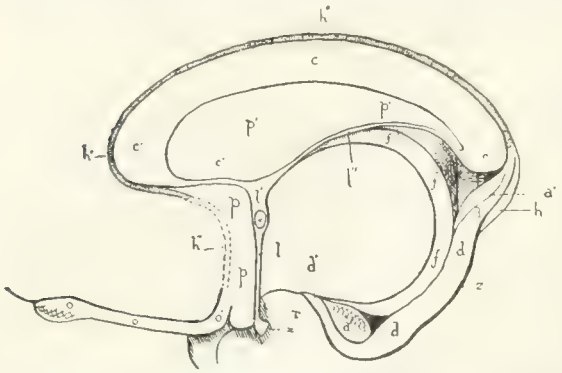

FIG. 970.—Scheme of the Cerebral Commissures and Margin of the Cortex in the Adult Human Brain. *a' a''*, Extraventricular alveus; *c c'*, corpus callosum; *d*, fascia dentata; *f f' f''*, fimbria; *h*, gyrus subsplenialis of Levi (gyrus Andreæ Retzii); *h''*, supracommissural hippocampus (vestigeal); *h'''*, precommissural hippocampus (vestigeal); *l*, lamina terminalis; *l' l''*, lamina supraneuroporica (Johnston); *o o'*, olfactory bulb and peduncle; *p*, precommissural body; *p'*, septum pellucidum; *r*, uncus (pyriform lobe); *s*, splenium of corpus callosum; *v*, anterior commissure; *x*, optic chiasma. (After G. Elliot Smith, from Johnston's Nervous System.)

FIG. 971.—Section through the Gyrus Hippocampi and Hippocampus (Cornu Ammonis) of the Adult Human Brain, taken so as to cut the Hippocampus Transversely. The relation of the gyrus dentatus to the cortex hippocampi is clearly indicated; also the continuity of the latter with that of the gyrus hippocampi and adjacent neopallium of the temporal lobe (*Gyrus occ. temp. inf.*). Both of the latter regions are connected with the hippocampus by association fibers in the alveus. A small portion of the gyrus dentatus appears on the surface, being separated from the subiculum of the gyrus hippocampi by the fissure hippocampi and from the cortex hippocampi and fimbria by the much shallower sulcus fimbrio-dentatus (visible bur not named on the figure). The plexus chorioideus of the lateral ventricle is drawn somewhat simpler than in nature. The way in which this membrane forms a part of the wall of the inferior horn of the lateral ventricle is clearly shown. (After Edinger.)

the layer of granules. In most vertebrates the lateral ventricles extend into the olfactory bulbs (rhinocele), but in the adult human brain this cavity is obliterated.

The olfactory fibers of the second order arise chiefly from the mitral cells and pass backward in three tracts, which form eminences or striæ at the base of the olfactory bulb, as follows (cf. Figs. 901 and 938).

(1) The stria lateralis discharges into the gyrus olfactorius lateralis, which extends backward through the limen insulæ to the uncus of the temporal lobe, these all constituting the area olfactoria lateralis (Fig. 953). Fibers of the third order, arising in the gyrus olfactorius lateralis, carry the impulse into the ventrolateral end of the hippocampus.

(2) The stria medialis discharges into the gyrus olfactorius medialis of Retzius (Fig. 953; this is the area parolfactoria of Broca, but not the lobus parolfactorius of Edinger which belongs in the area olfactoria intermedia) and the gyrus subcallosus, septum, etc.; *i.e.* the area olfactoria medialis, as above defined. From this area fibers of the third order pass in different directions. The most primitive and the largest connection is directly backward through the

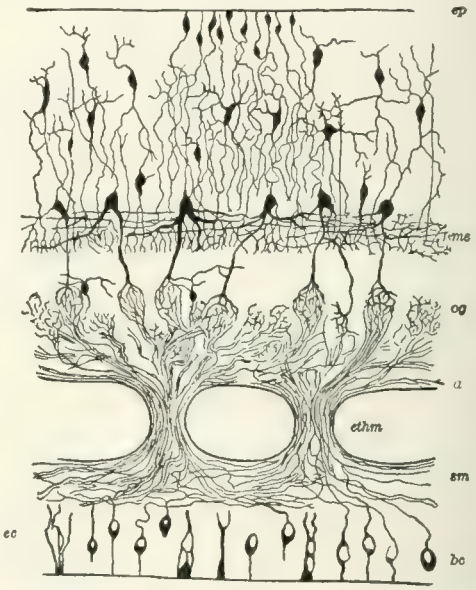

FIG. 972. Diagram of the Structure of the Olfactory Mucosa of the Nose and the Formatic Bulbaris of the Olfactory Bulb. *a*, layer of olfactory nerve fibers; *bc.*, bipolar cells (specific olfactory receptors) of the olfactory mucosa; *ep.*, ependyma of the olfactory ventricle; *ethm.* cribriform plate of the ethmoid bone; *me.*, mitral cells; *og.*, olfactory glomeruli; *sm.*, submucosa. (After Ramón y Cajal, from Bailey's Histology.)

great basal olfactory tract to the hypothalamus and midbrain (Fig. 973, *tr. olf. hypth.*). Another extensive series of fibers, the tractus olfactorius septi, ascends through the septum to the fimbria under the corpus callosum, thence passing into the dorsal end of the subcommissural hippocampus. A smaller number of fibers carry impulses upward around the rostrum of the corpus callosum to the indusium of the callosum, and by way of the striæ Lancisii around the splenium of the callosum to the dorso-medial end of the subcommissural hippocampus. It will be recalled that the indusium griseum of the corpus callosum is the surviving vestige of the large horizontal limb of the hippocampus (cf. Figs. 959 and 960), which has been reduced by the development of the corpus callosum. This gives the explanation of the aberrant course of the central olfactory tract through the striæ Lancisii.

(3) Between the lateral and medial olfactory striæ an intermediate system of fibers passes backward from the olfactory crus to enter the gyrus olfactorius intermedius in the anterior perforated space. This region contains the equivalent of the tuberculum

olfactorium of lower mammals and receives uncrossed fibers of the second order from the olfactory bulb and also a part of the large tractus olfactorius intermedius which first decussates in the anterior commissure. It is said by Edinger also to receive important ascending fibers from the trigeminus region of the thalamus for the correlation of tactile and other stimuli connected with the nose and lips and olfactory impressions.

The intermediate area, like the medial, sends backward into the hypothalamus and tegmentum a large basal olfactory tract, which probably serves for the simpler olfactory reactions. It also sends a large component into the tractus olfactorius septi, which runs through the septum into the fimbria to reach the dorsomedial part of the hippocampus for cortical olfactory reactions. Both the medial and intermediate areas give rise to another large tract which ascends across the anterior face of the thalamus to reach the habenula in the epithalamus. This tractus olfactohabenularis is the most important component of the stria medullaris thalami.

The stria medullaris thalami is a very complex tract whose fundamental characteristic can be stated very simply. That is, it is a conduction pathway by which fibers arising in all parts of the rhinencephalon are led to their termination in the epithalamus. Some of these fibers terminate in the habenula of the same side; others first decussate in the superior, or habenular, commissure, to reach the habenula of the opposite side. In primitive vertebrates (cyclostome fishes), where the olfactory area is simply organized and relatively homogeneous, fibers of this system stream backward from all parts of it quite uniformly, to converge in the habenula. But with the analysis in higher forms of the primordial olfactory area into functionally diverse parts, as outlined above, and their wide separation, some of the components of the stria medullaris which arise from these several parts take very devious courses before they are assembled in the diencephalon. The stria medullaris, as thus constituted, takes a superficial course across the anterodorsal face of the thalamus near the middle plane and accompanying the tænia thalami (Figs. 948, 973). It is sometimes termed the tractus tænia, or tænia thalami, though the latter term is reserved by the BNA for the line of attachment of the membranous roof to the massive wall of the thalamus (Fig. 968, *t. th.*).

A tolerably complete analysis of the stria medullaris has been made in the case of some fishes and amphibians (Johnston, Sheldon, Herrick, etc.); but there is no agreement as to its composition in the mammals. On the basis of a still unpublished investigation made in my laboratory by Dr. F. A. C. Perrin, I am able to give the following summary of the composition of the stria medullaris in the white rat.

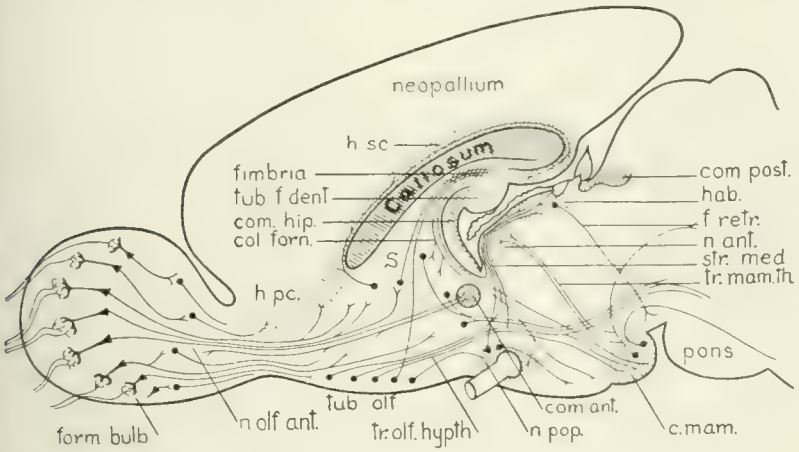

FIG. 973.—Diagram of Some of the Olfactory Tracts in the Brain of the Rat. The chief connections of the medial and intermediate olfactory tracts are indicated; those of the lateral olfactory tract are omitted. *c. mam.*, Corpus mammillare; *col. forn.*, columna fornicis; *com. ant.*, commissura anterior; *com. hip.*, commissura hippocampi; *com. post.*, commissura posterior; *form. bulb.*, formatio bulbaris; *f. retr.*, fasciculus retroflexus of Meynert; *hab.*, habenula; *h. pc.*, hippocampus pre-commissuralis; *h. sc.*, hippocampus supracommissuralis; *n. ant.*, nucleus anterior thalami; *n. olf. ant.*, nucleus olfactorius anterior; *n. pop.*, nucleus preopticus (ganglion opticum basale); *S.*, septum; *str. med.*, stria medullaris thalami; *tr. mam. th.*, tractus mammillo-thalamicus (Vicq d'Azyri); *tr. olf. hypth.*, tractus olfacto-hypothalamicus, or basal olfactory tract; *tub. f. dent.*, tuberculum fasciæ dentatæ (hippocampus postcommissuralis; *tub. olf.*, tuberculum olfactorium.

(1) Tractus olfactohabenularis medialis. From the preoptic nucleus (ganglion opticum basale) to the habenula. These fibers arise from the entire region about the optic chiasma in several fascicles. There is an anterior part running up in front of the columna fornicis (shown in Fig. 973) and a posterior part arising behind the columna fornicis, whose connections are not entirely clear. Honegger has described a tractus olfactohabenularis lateralis, arising from this region and passing up laterally of the internal capsule system of fibers. This occurs in amphibians and reptiles and probably in mammals also, though we have not been able to demonstrate it.

(2) Tractus olfactohabenularis anterior. In the rat this is the largest component of the stria medullaris. Its fibers arise from the tuberculum olfactorium, pass caudad mingled with those of the great basal olfactory projection tract (Fig. 973, *tr. olf. hypth.*) and at the level of the optic chiasma turn dorsally to join those of component 1.

(3) Tractus septohabenularis. These fibers arise from the entire septum and precommissural body, particularly in the vicinity of the anterior commissure.

(4) Tractus corticohabenularis medialis. Fibers arising in the hippocampus and passing out through the fimbria and columna fornicis leave the latter above the anterior commissure to enter the stria medullaris (Fig. 973).

(5) Tractus corticohabenularis lateralis. This component is very large in amphibians and reptiles, arising in the region of the pyriform lobe. It has never been identified in mammals. We find that the stria terminalis, which passes between the nucleus amygdalæ (under the pyriform lobe) and the septum, contributes fibers to the stria medullaris where these two systems cross near the medial plane above the anterior commissure. This connection was probably observed by Honegger in 1890, but seems to have been since overlooked; it probably represents a pathway from the amygdala to the habenula, and therefore is the equivalent of the tractus corticohabenularis lateralis as described in lower vertebrates.

(6) Tractus thalamohabenularis. Fibers pass from the nucleus anterior thalami through the stratum zonale thalami into the stria medullaris.

(7) Tractus striohabenularis. Fibers pass between the stria medullaris and the medial part of the globus pallidus of the corpus striatum. Their connections are unknown. They may contain the descending fibers from the habenula which some authors have described in the stria medullaris.

In addition to the preceding, there are also less

perfectly understood connections between the habenula and the thalamus and midbrain.

Another important association tract of the rhinencephalon is the stria terminalis (also called the tænia or stria semicircularis and stria cornea, though the best usage would apply the latter name to a thick band of non-nervous tissue which accompanies the nerve fibers). This system puts the lateral olfactory area into relation with the medial and intermediate areas. In reptilian brains these fibers pass simply across the basis of the hemisphere in the transverse plane between the medial and lateral olfactory areas, lying beneath the lateral ventricle and above the internal capsule system of fibers. But in mammals the great increase in size of the internal capsule system has necessitated a wide backward loop across the dorsal and posterior border of this system of fibers. From this it results that the stria terminalis appears as a well-defined ridge extending across the dorsal surface of the brain stem from the lamina terminalis (Fig. 938, *Tænia semicircul.*) obliquely backward and lateralward, as seen in Fig. 975. Here it marks the boundary between the thalamus and the corpus striatum and lies parallel with the vena terminalis and the line of attachment of the plexus chorioideus lateralis of the hemisphere to the tænia chorioidea, the latter, however, lying farther medialward being separated from the stria terminalis by the lamina affixa (see beyond under *Meninges*, and Fig. 995). Behind the plane of contact of the thalamus with the corpus striatum the stria terminalis turns ventralward, forward, and lateralward to connect with the nucleus amygdalæ under the uncus of the temporal lobe (Fig. 987).

The olfactory cortex (cortex hippocampi and gyrus dentatus) receives olfactory tracts from the lateral area olfactoria at its ventro-lateral end from the region of the uncus, and also from the medial and intermediate areas at the dorso-medial end of the undegenerated (postcommissural) hippocampus through the septum and fimbria by way of the tractus olfactorius septi.

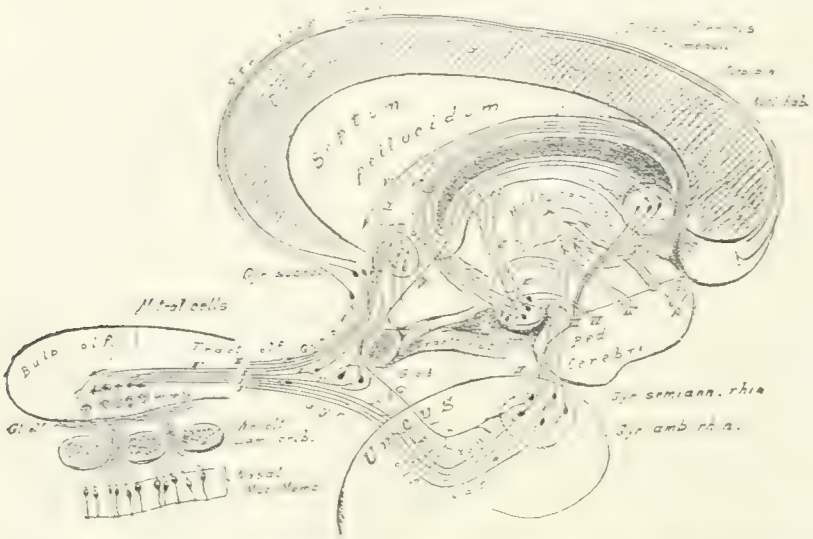

FIG. 974.—Schematic Representation of Some of the Principal Neurone Systems of the Olfactory and Habenula Paths. Projected into sagittal plane. *Bulb. olf.*, bulbus olfactorius; *Cal. fasc.*, calcarina fasciculus; *Comm. ant.*, commissura anterior cerebri; *Corp. mam.*, corpus mammillare; *Corp. pin.*, corpus pineale; *G. o. b.*, ganglion opticum basale; *Gl. olf.*, glomeruli olfactorii; *Gyr. amb. rhin.*, gyrus ambiens rhinencephali; *Gyr. olf. lat.*, gyrus olfactorius lateralis; *Gyr. o. m.*, gyrus olfactorius medialis; *Gyr. semiann. rhin.*, gyrus semilunaris rhinencephali; *Gyr. subcall.*, gyrus subcallosus; *Lam. crib.*, lamina cribrosa; *N. a. th.*, nucleus anterior thalami; *Nn. olf.*, nervi olfactorii; *Nucl. hab.*, nucleus habenulæ; *Ped. cerebri*, pedunculus cerebri; *Str. long. med.*, stria longitudinalis medialis; *Str. medull.*, stria medullaris; *Tract. olf.*, tractus olfactorius; *Tract. opt.*, tractus opticus; *I*, axones of mitral cells going to stria olfactoria lateralis; *I'*, axone of mitral cell terminating in gray matter of trigonum olfactorium; *II*, axone of mitral cell terminating in gray matter, whence axone goes to commissura anterior cerebri; *II'*, axones to anterior commissure; *II''*, centrifugal fiber terminating in bulbus olfactorius; *III*, axone of mitral cell terminating in gyrus olfactorius medialis; *IV*, axones of neurones connecting the olfactory portion of the uncus (gyrus ambiens and gyrus semilunaris) with the hippocampus (cornu ammonis); *V*, axones from hippocampus to fornix; *V'*, axone to commissura hippocampi; *V''*, axones from fornix to septum pellucidum; *V'''*, axones from fornix to corpus mammillare; *V''''*, axone from fornix to nucleus habenulæ by way of the stria medullaris; *VI*, fasciculus mammillaris princeps; *VI'*, fasciculus thalamo-mammillaris Vicq d'Azyri; *VI''*, fasciculus pedunculo-mammillaris, pars tegmentalis (*Haubenbündel* of von Gudden); *VII*, fasciculus pedunculo-mammillaris, pars basilaris (pedunculus corporis mammillaris); *VIII*, fasciculus retroflexus Meynerti extending from the nucleus habenulæ to the nucleus interpeduncularis. (After Barker, from "The Nervous System and Its Constituent Neurones," D. Appleton & Co., 1900.)

The efferent path from the hippocampus follows the fimbria (in the reverse direction from the afferent fibers of the tractus olfactorius septi from the medial olfactory area) as far as the lamina terminalis, where it curves ventrally above the anterior commissure and then backward through the diencephalon to enter the corpus mammillare of the hypothalamus and adjacent parts of the tuber cinereum. This is the columna fornicis (Figs. 948, 973, 974). A part of the fornix fibers, however, separate from the others immediately behind the lamina terminalis and turn abruptly dorsally to enter the stria medullaris thalami and terminate in the habenula of the epithalamus, thus constituting the tractus cortico-habenularis medialis.

The accompanying diagram (Fig. 973) illustrates the chief connections of the rhinencephalon in the rat, where this system is relatively much more highly developed than in man; and Fig. 974 presents some of the more important olfactory connections in the human brain. In these diagrams it will be observed that both the cortical and the subcortical parts of the rhinencephalon discharge backward into the hypothalamus through the fornix and basal olfactory tract respectively and into the epithalamus through the stria medullaris thalami.

From the epithalamus the chief descending path is by way of Meynert's fasciculus retroflexus to the nucleus interpeduncularis in the floor of the midbrain. From the hypothalamus there are several descending tracts to the pedunculus cerebri and tegmentum. The latter are accompanied by fibers of the second order which pass directly back from the medial and intermediate olfactory areas without being interrupted in the corpus mammillare. The descending fibers from the mammillary body give off collateral branches to form the tractus mammillothalamicus (commonly called the tr. thalamo-mammillaris, or Vicq d'Azyr's bundle), which ends in the nucleus anterior thalami. Here the olfacto-visceral functions of the hypothalamus are correlated with the somatic functions of the thalamus. The nucleus anterior is also related to the habenula by a com-

ponent of the stria medullaris thalami, the tractus thalamohabenularis.

The reason for the division of the descending olfactory pathway into two systems related with the hypothalamus and the epithalamus respectively is not altogether clear. The most probable hypothesis is that the ventral path is concerned in the hypothalamus with olfacto-visceral correlations, while the dorsal path into the epithalamus is concerned with the correlation of olfactory impressions with the somatic sensory functions of the thalamus and midbrain. The olfacto-somatic correlations here effected are undoubtedly of different physiological type from those effected in the nucleus anterior thalami which receives its olfactory fibers, not directly from the telencephalon, but indirectly through Vicq d'Azyr's bundle from the hypothalamus, where they are first brought into physiological relation with manifold visceral (and gustatory?) associations of the hypothalamic nuclei. All of the relations of the nucleus anterior suggest that it is to be grouped with the medial series of thalamic nuclei, concerned chiefly with intrinsic visceral thalamic functions, rather than with the lateral series of cortical dependencies (Sachs).

It is a well-known fact, which has been emphasized by Sherrington, that the sense of smell has a two-fold function; first, the excitation of visceral reactions (interoceptive) in connection with feeding and the discrimination of food substances, etc., in the mouth, and, second, the excitation of somatic responses, *e.g.* locomotion, when distant objects are smelled (exteroceptive, distance reactions). The neurological mechanism of coordination concerned in these two types of response would necessarily be very different, and it is probable that the hypothalamus serves the interoceptive and the epithalamus the exteroceptive series.

The Corpus Striatum.—The somatic part of the cerebral hemisphere comprises the corpus striatum and the neopallium. The corpus striatum arises from the ventro-lateral wall of the cerebral hemisphere vesicle (Figs. 887, 896, 954, 956). In later developmental stages the pallium completely envelops it except on the ventricular side, where it forms in the adult a strong eminence projecting into the lateral ventricle. It is traversed by massive tracts of projection fibers between the neopallium and the lower centers. These projection fibers in part pass laterally of the corpus striatum as external capsule fibers and in part through its substance and between it and the thalamus, thus forming the internal capsule. The internal capsule separates the corpus striatum into a medial gray mass, the nucleus lentiformis (with two subdivisions, putamen and globus pallidus), and a lateral comma-shaped mass, the nucleus caudatus, whose enlarged head is situated far forward forming the lateral wall of the anterior horn of the lateral ventricle (Fig. 975) and whose attenuated posterior part follows the stria terminalis to end in the nucleus amygdalæ under the uncus of the temporal lobe.

The intrinsic fiber connections of the corpus striatum are still somewhat obscure, because these fibers are so mingled with those of the projection systems of the cerebral cortex as to make their separation difficult. There is a broad striothalamic connection consisting of both ascending and descending fibers between all parts of the corpus striatum and the thalamus. Some of these fibers pass farther back to the mesencephalon. There is also a special ascending tract from the nucleus anterior thalami to the head of the caudate nucleus (Sachs), and the latter is in intimate relation with the underlying intermediate olfactory area in the anterior perforated space.

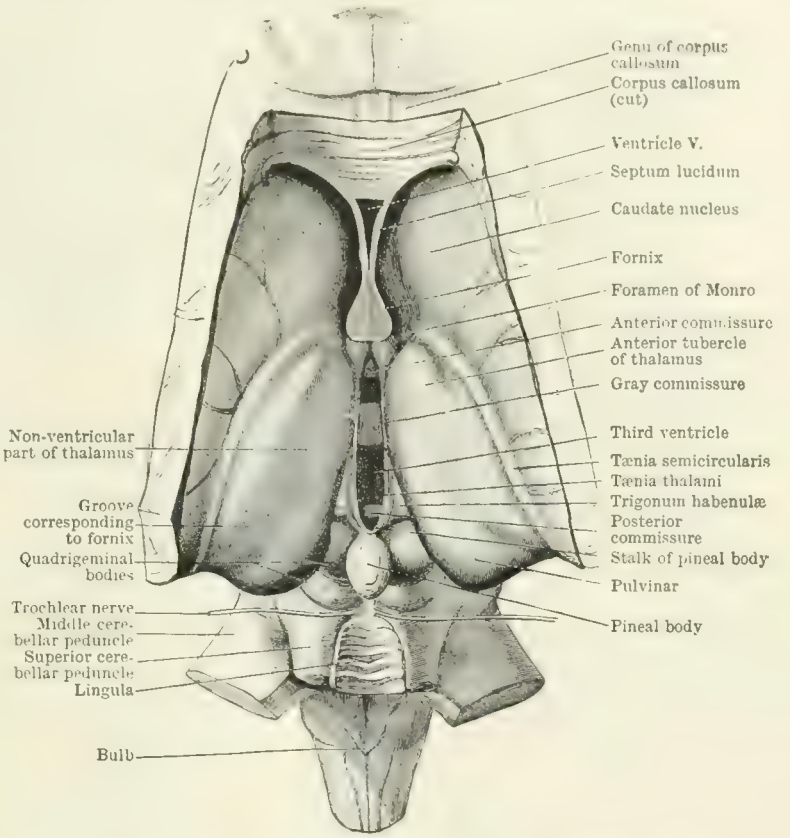

Fig. 975.—A Dissection of the Brain from Above to expose the Optic Thalami and Corpus Striatum. (From Cunningham's Anatomy.)

Ramón y Cajal teaches that the corpus striatum is the anterior member of a series of motor correlation centers which is continued backward into the nuclei of the subthalamic region and the substantia nigra. These all receive collaterals of the fibers of the pyramidal tract and serve to reinforce the descending motor impulses from the cerebral cortex, as well as to effect local reflex responses of subcortical type.

Neopallium.—Practically all of the exposed cerebral cortex of the adult human brain belongs to the neopallium. The early stages of the histogenesis of the cortex are similar to those of other parts of the neural tube, though somewhat later in their appearance. The thickening in the ventro-lateral region destined to form the corpus striatum begins about the end of the first month and after another month the cortical layer first begins to appear superficially of the corpus striatum. Fig. 976 illustrates the histogenetic development of the wall of the hemisphere at the beginning of the third month, at which time a distinctive cortical layer has begun to appear. The process of the differentiation of the

outer cortical layer advances from the lateral toward the medial border of the cortex. In a fetus of the third month (Fig. 977) the cortical layer has reached as far as the fissura arcuata, but not across this fissure to the extreme medial margin of the pallium at the tænia fornicis. The medial border therefore exhibits at this age a limbus corticalis, which marks the limit of differentiated cortex, and beyond this a limbus medullaris devoid of cortex. The limbus medullaris never becomes wholly transformed into cortex, but its marginal part becomes filled with the fibers of the fimbria.

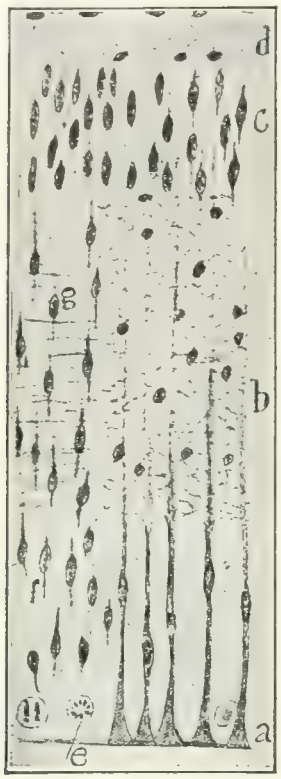

Fig. 976.—Section through the Pallial Wall of a Human Fetus at the Beginning of the Third Month. *a*, Internal limiting membrane; *b*, fibrous (medullary) layer; *c*, layer of neuroblasts forming rudimentary cortical gray matter; *d*, marginal layer (future molecular layer); *e*, germinal cell *f.g.*, neuroblasts with radial processes; spongioblasts and myelospongium are shown on the right side. (After His, from Bailey and Miller's Embryology.)

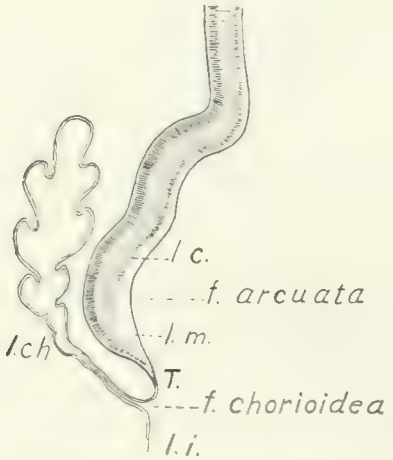

Fig. 977.—Margin of the Cerebral Hemisphere (Limbus Hemisphæri) of the Human Fetus of Three Months. *l. c.*, Limbus corticalis; *l. ch.*, lamina chorioidea; *l. i.*, lamina infrachoriodea; *l.m.*, limbus medullaris; *T.*, tænia fornicis. (After His.)

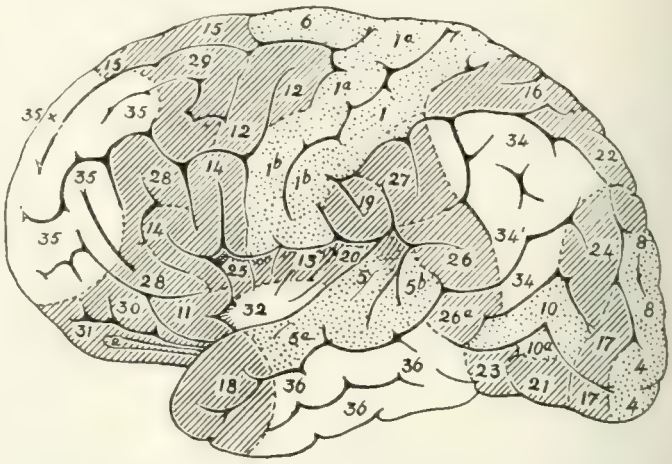

Fig. 978.—Diagram of the Cortical Areas of the Lateral Surface of the Cerebral Hemisphere, as Determined by the Myelogenetic Method. The numerals indicate in a general way the order of myelination. The primary areas (1–10) are indicated by dots, the intermediate areas (11–31) by oblique lines, and the terminal or final areas (32–36) by clear spaces. (After Flechsig, from Quain's Anatomy.)

In the third month fibers of the thalamic radiations (sensory projection fibers) appear in the medullary layer of the cortex. In later development cortical neurones give rise to descending projection fibers and to association tracts connecting different parts of the cortex. The latter process continues up to adult life.

Further differentiation of the wall of the cerebral hemisphere involves the rapid thickening of the medullary layer (white matter) and the arrangement of the cells and fibers of the cortex into more or less definite layers. The sequence of medullation of the nerve fibers of the cortex has been studied with great care by Flechsig. Certain areas acquire their medullated fibers much earlier than others, related functional connections tending to appear at the same time. Figs. 978 and 979 give a summary view of some of the results of these researches. His (1904) has given an excellent table of the sequence of the first appearance of many of the important tracts of the brain.

The first cerebral fissures to develop, as we have already seen, are those separating the rhinencephalon from the neopallium. In the third month the fissura prima (His) appears, forming the anterior boundary of the Trapezfeld of His (precommissural body of Elliot Smith). A portion of this fissure on the ventral surface is preserved in the adult as the sulcus parolfactorius posterior. In the third month the lateral rhinal fissure and the hippocampal fissure (fissura arcuata) are well defined. At about this time the accessory arcuate and the calcarine fissures appear on the medial surface (Fig. 955) and the Sylvian fissure on the lateral surface (Fig. 980). At this age numerous transitory fissures are present, most of which, like the accessory arcuate, disappear in the adult. The calcarine fissure is preserved as a total fissure, the ventricular eminence which it forms being the calcar avis (hippocampus minor). At the beginning of the fourth month the calcarine fissure is joined by the parieto-occipital fissure, thus delimit-

ing the cuneus. The posterior part of the arcuate fissure is also preserved as a total fissure, the fissura hippocampi, and its ventricular eminence is the hippocampus (cornu Ammonis). The anterior part occupies the corresponding position (callosal fissure) has an independent origin.

Although the cortex begins to differentiate over the corpus striatum, yet in later stages its develop-

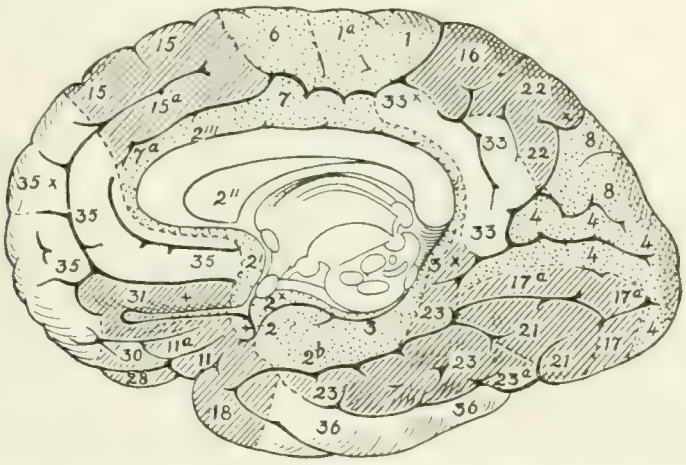

Fig. 979.—Diagram, Similar to Fig. 978, of the Medial Surface of the Hemisphere. (After Flechsig, from Quain's Anatomy.)

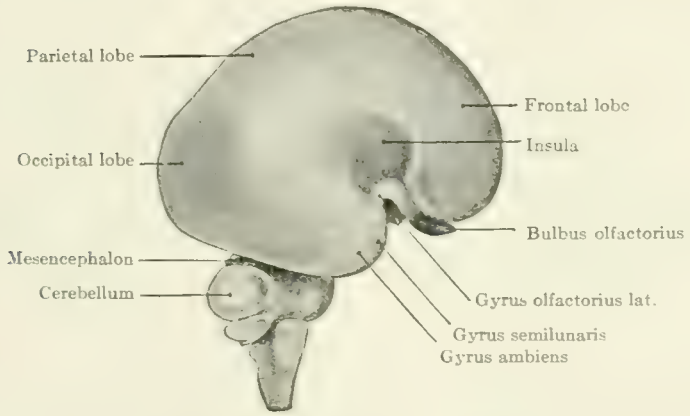

Fig. 980.—Lateral View of the Brain of a Human Fetus at the Beginning of the Fourth Month. (After Kollmann, from Bailey and Miller's Embryology.)

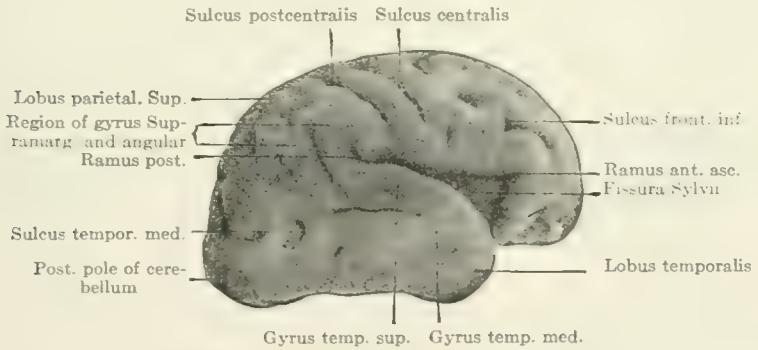

Fig. 981.—Lateral View of the Right Cerebral Hemisphere of a Human Fetus at the End of the Seventh Month. (After Kollmann, from Bailey and Miller's Embryology.)

of the fissura arcuata, which corresponds with the horizontal limb of the hippocampal fissure of marsupials (Fig. 957), is said by Cunningham to disappear in the human embryo and the adult fissure which ment is retarded in this region. Thus arises the fossa lateralis Sylvii, whose floor is the future insula and whose walls become the opercula (Figs. 980, 981). It thus appears that the lateral fissure (fissure of

Sylvius), which is the most conspicuous fissure of the hemisphere, is not a total fissure, involving the whole thickness of the wall, like the fissura hippocampi and the fissura calcarina. In the adult brain the fissure

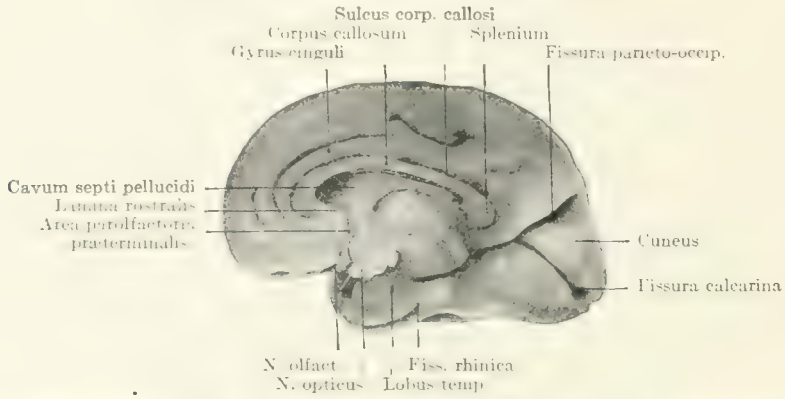

FIG. 982.—Medial View of the Right Half of the Brain of a Human Fetus at the End of the Seventh Month. (After Kollmann, from Bailey and Miller's Embryology.)

of Sylvius has three main branches arising from a common stem, the anterior and posterior horizontal and an anterior ascending (Fig. 985). The lips of the three limbs of the Sylvian fissure form the operand do not come into apposition until after birth. Fig. 984 gives a diagrammatic representation of the mode of development of these opercula, after Cunningham, who adds the following comments:

"The orbital operculum appears first and is much more constant in its growth than the frontal operculum, which indeed frequently fails altogether, and, even when present, shows the greatest amount of

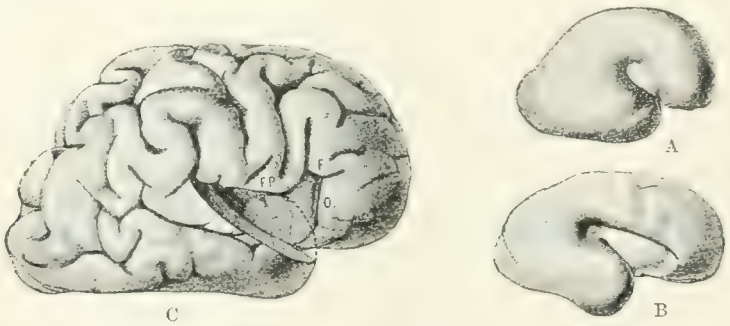

FIG. 983.—Three Stages in the Development of the Insula and the Insular Opercula. *A*, Right cerebral hemisphere from a fetus in the latter part of the fourth month of development; *B*, right cerebral hemisphere from a fetus in the fifth month; *C*, right cerebral hemisphere from a fetus in the latter part of the eighth month. In *C* the temporal operculum has been removed and thus a large part of the insula is exposed. The outline of the temporal operculum is indicated by a dotted line. *F.*, frontal operculum; *F. P.*, fronto-parietal operculum; *O.*, orbital operculum. (From Cunningham's Anatomy.)

cula of the island of Reil, which is a buried convolution surrounded by the limiting sulcus of Reil and entirely invisible in the intact adult brain. The limbs of the Sylvian fissure bound the opercula (Fig. 983), viz., variability in the degree to which it is developed. Variations in the degree of development of the frontal operculum influence greatly the form presented by the two anterior limbs of the Sylvian

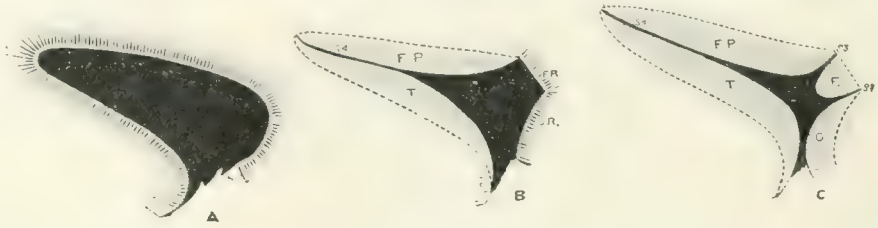

FIG. 984.—A diagram to Illustrate the Development of the Opercula which Cover the Insula. A, Sylvian fossa before the opercula begin to form; B, fronto-parietal and temporal opercula well advanced; C, all four opercula developed but not in apposition; *F.*, frontal operculum; *F.P.*, fronto-parietal operculum; *F. R.*, frontal wall of fossa; *O.*, orbital operculum; *O.R.*, orbital wall of fossa; S^2., anterior horizontal limb of Sylvial fissure; S^3., ascending limb; S^4., posterior horizontal limb; *T.*, temporal operculum. (From Cunningham's Anatomy.)

the temporal, fronto-parietal, frontal and orbital operculum. The temporal and fronto-parietal opercula begin to appear about the end of the fifth month; the orbital and frontal opercula develop much later fissure, between which it lies. When strongly developed, it separates the two Sylvian limbs from each other to such an extent that they assume the appearance of the letter U; when the frontal opercu-

lum is less strongly marked, the anterior Sylvian limbs may assume a V form or a Y form. In the latter case, the orbital and fronto-parietal opercula meet below the frontal operculum to form the stem of the Y. In those cases where the frontal operculum is absent altogether, a single anterior limb of the Sylvian fissure is the result. The late appearance, the slow growth, the variability of these two opercula and also the tendency to abortive growth or complete suppression of the frontal operculum, all bespeak the fact that, from a phylogenetic point of view, the frontal and orbital opercula are, comparatively speaking, recent productions in the evolution of the human brain. In the anthropoid ape they are absent, and, consequently, the fore part of the island of Reil is exposed on the surface of the simian brain. The same condition is not at all an uncommon occurrence in the brain of the microcephalic idiot." These considerations are of interest in connection with the occurrence of the motor speech centers (Broca's region) in the opercula.

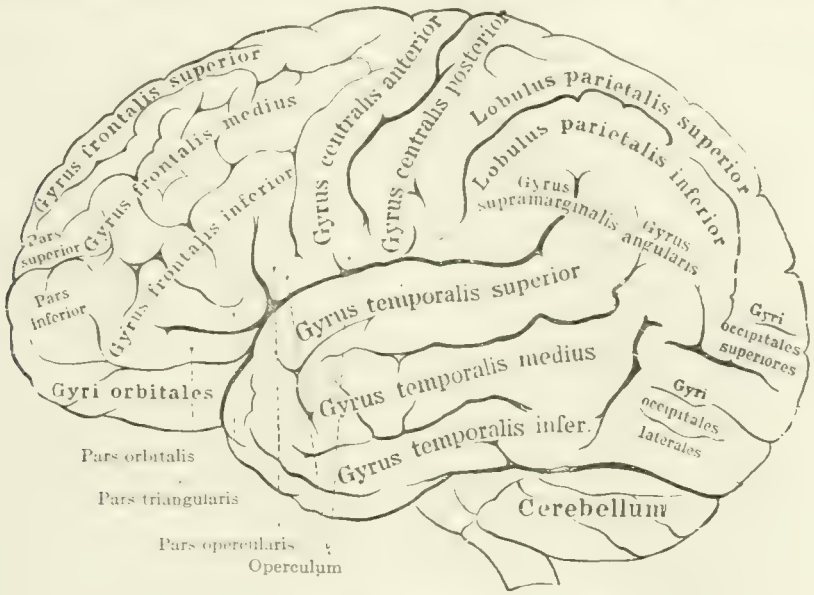

Fig. 985.—Lateral View of the Left Cerebral Hemisphere, Illustrating the Chief Gyri and Sulci. After Toldt.

In early stages of the development of the hemisphere many transitory fissures appear, some of which, like the accessory arcuate, are very constant, while others are variable. After the fourth month the permanent fissural pattern is rapidly laid down.

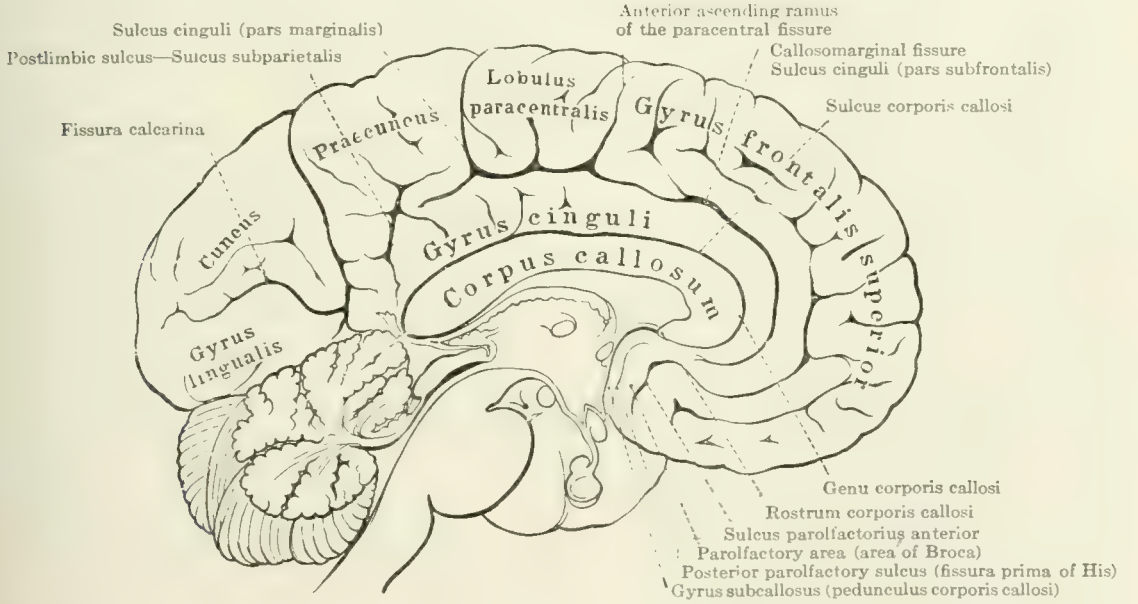

Fig. 986.—Medial Surface of the Left Cerebral Hemisphere, Illustration the Gyri and Sulci. (After Toldt.)

Figs. 981 and 982 illustrate their arrangement in the seventh month.

The adult hemisphere has been mapped out into definite areas characterized by differences in the structure and lamination of its cortical cells and fibers. The relation between these areas, which are doubtless functionally determined, and the fissural pattern is controverted; but there is a sufficiently close correspondence between the most important cortical areas and the early cerebral fissures to suggest that the positions of the latter are determined, in part at least, by inequalities in the time of development of the functionally defined regions. Flechsig's studies on the medullation of cortical fiber tracts also give some support to this view.

The arrangement of the principal sulci and gyri of the cerebral hemisphere is shown in Figs. 985 and 986.

The fasciculus longitudinalis superior (*f. l. s.*) connects the frontal, occipital and temporal regions of the hemisphere. The fasciculus longitudinalis inferior (*f. l. i.*) extends along the whole length of the occipital and temporal lobes. The fasciculus occipito-frontalis (not shown on the figure) runs lengthwise of the hemisphere bordering the ventricle and the caudate nucleus on the inner aspect of the corona radiata. The fasciculus occipito-frontalis inferior (*f. occ. fr. inf.*; see Curran, *Jour. Comparative Neurology*, vol. xix., 1909) unites the frontal lobe with the occipital and posterior parts of the temporal and parietal lobes and lies farther ventral than the last. The cingulum (*cin.*) is a very well-defined bundle which borders the corpus callosum near the medial plane and connects all parts of the limbic lobe (olfactory association centers bordering the hippocampus, etc.). The fasciculus uncinatus (*f. unc.*) connects the anterior

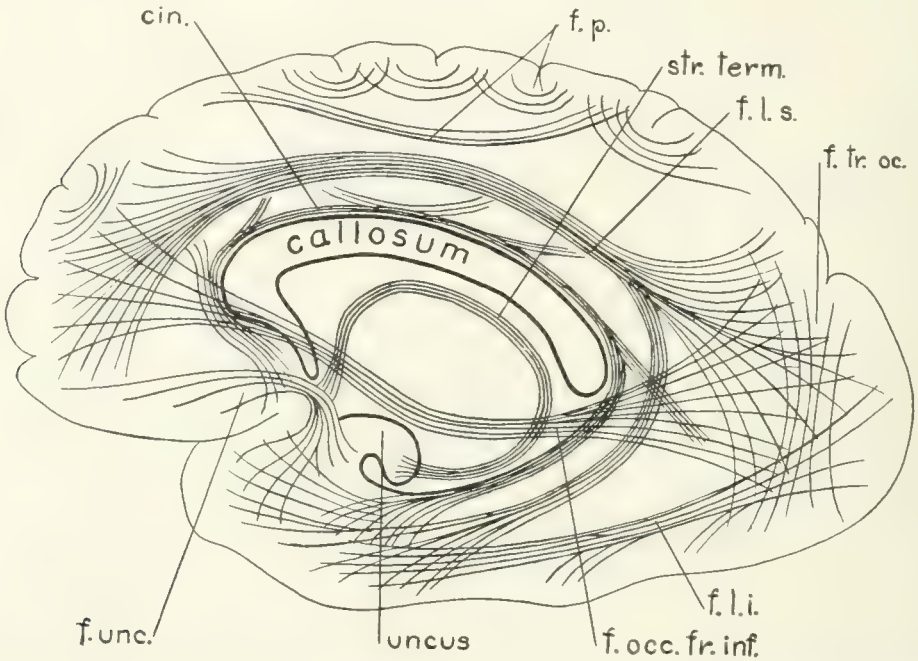

Fig. 987.—Diagram Illustrating Some of the Chief Association Tracts of the Cerebral Hemisphere, seen as Projected upon the Mesial Surface of the Right Hemisphere. *cin.*, Cingulum; *f.l.i.*, fasciculus longitudinalis inferior; *f.l.s.*, fasciculus longitudinalis superior; *f. occ. fr. inf.*, fasciculus occipito-frontalis inferior; *f.p.*, fibræ propriæ; *f. tr. oc.*, fasciculus transversus occipitalis; *f. unc.*, fasciculus uncinatus; *str. term.*, stria terminalis.

Sensory projection fibers from the different thalamic nuclei pass upward through the internal capsule to reach the cortical areas devoted respectively to vision, hearing, cutaneous sensibility, etc. Other fibers arise from cells of the motor projection centers in the precentral convolution (gyrus centralis anterior) and adjacent parts and descend through the pyramidal tract to effect connection with lower motor centers. Between the sensory and motor projection centers which are thus defined are intercalated the association centers which are connected by an elaborate system of subcortical fibers with the projection centers and with each other. In the developing brain, as we have already seen (Figs. 978, 979), the projection fibers in general mature earlier than do the association fibers.

Each gyrus is connected with those immediately contiguous by short superficial arcuate fibers and with more remote gyri by deeper association tracts. The principal association centers are connected by massive bundles of such fibers which can easily be dissected out in a well preserved brain (Fig. 987).

end of the temporal lobe with the frontal lobe. The fibræ propriæ (*f. p.*) are short association fibers forming the more superficial layers of the white matter.

The histological structure of the cortex differs in the various regions and much study has of late been devoted to the precise nature and significance of these differences. Both the fibers and the cells of the cortex show a more or less evident lamination and these layers are variously constituted in different areas. Elliot Smith has shown that these differences in lamination are sufficiently evident in gross preparations of fresh brains as to permit the delimitation of the structural regions demonstrated by the histological studies of Campbell, Brodmann, etc., with a fair degree of precision.

Authors classify the cortical layers differently. Bolton's researches have suggested to him that the cellular elements are arranged in three fundamental layers throughout the cortex. The deepest layer of cells (polymorphous cells) is the first to be differentiated and it is the last to fail in the retrogressions of dementia. The middle, or granular layer is the

next to appear, while the outer, or pyramidal cell layer is the last to develop and it is also the first to undergo retrogression in dementia. Bolton is inclined to associate the psychic or higher associational functions of the cortex with the pyramidal layer, the reception and immediate transformation of afferent impressions with the middle layer and the lower impulsive functions of the vegetative life with the deepest layer. This interpretation, however, is not universally accepted and there is controversy as to whether any functional analysis of the cortex in terms of layers is practicable.

Brodmann distinguishes six cortical layers which are differentiated during the seventh month: (1) external molecular layer, (2) external granular layer (layer of small pyramids), (3) pyramidal layer (medium and large pyramids), (4) internal granular layer, (5) ganglionic layer (internal pyramids), (6) polymorphic cells. The second and third of these layers constitute Bolton's outer layer, the fourth his middle layer and the fifth and sixth his inner layer. Campbell in the adult recognizes seven layers of cells, dividing Brodmann's third layer into two. Ramón y Cajal also enumerates for the cortex in general seven layers, these being similar to Brodmann's save that the fifth layer is divided into two. The medullated fibers of the cortex in the adult are also arranged in layers which have been variously subdivided. The arrangement of both the cells and the fibers differs in different parts of the cortex, and on the basis of these differences various authors have mapped out the cortical areas of like lamination and cellular pattern. The most extensive of these studies are those of Brodmann and Campbell (see Fig. 988). The details of cortical localization and function are treated in other articles in this Handbook.

Fig. 989 presents a diagram by Dr. O. S. Strong of some of the more important somatic sensorimotor functional connections of the neopallium and brain stem as seen from the left side of the brain. This scheme will serve in the place of an extended summary of the chief architectural features (except the olfactory system, for which see Fig. 973), which we have discussed in this article.

The Significance of the Cerebral Cortex.—In the spinal cord and oblongata the correlation tissue is developed within the segments without great distortion of their primitive segmental pattern, to serve the simpler stereotyped and innate reactions of the reflex type. The simplest form of this correlation tissue is known as the reticular formation and serves to put the primary receptive centers into physiological relation with the efferent nerve centers in the same and other segments. The neurones of the reticular formation are so arranged as to provide definite pathways for the more common types of reflex discharge and coordination. Within it certain gray masses like the olives and the pontile nuclei are highly differentiated to serve special combinations of reflexes. The axones of some of these cells form compact medullated fiber tracts, such as the fasciculus longitudinalis medialis and the central bundle of the tegmentum, to connect remote parts of this system of correlation centers. The cerebellum and the larger nuclei of the thalamus represent more elaborate correlation centers of this sort developed above and quite independently of the primary metamerism, thus constituting the suprasegmental coordination centers of Adolf Meyer. And the cerebral cortex is

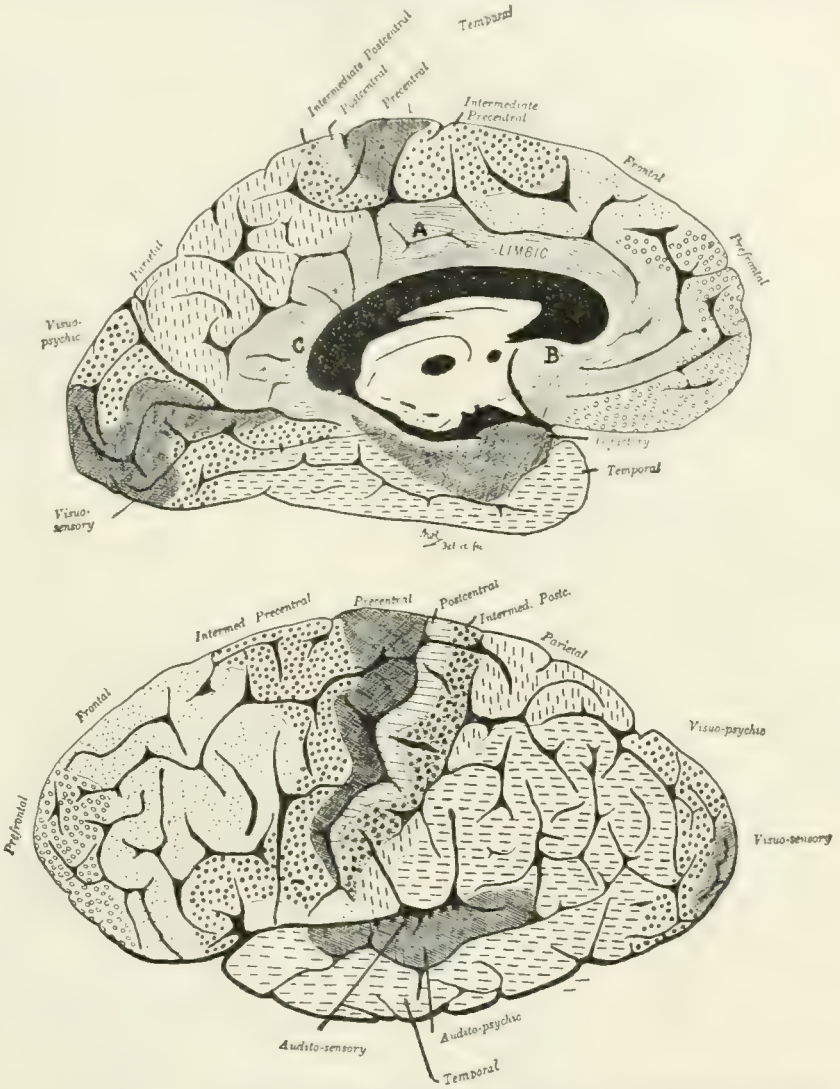

Fig. 988.—Diagrams of the Lateral and Medial Surfaces of the Cerebral Hemisphere, Illustrating the Limits of the Cortical Areas as Determined by the Arrangement and Distribution of Fibers and Cell Lamination. Large portions of important areas are concealed within fissures, *e.g.*, the calcarine or visual (Visuo-sensory within the calcarine fissure), the precentral (motor), and postcentral (within the central sulcus or fissure of Rolando), and especially the acoustic (Audito-sensory), which is almost completely hidden within the Sylvian fissure. *A*, *B* and *C* are parts of the limbic lobe. (After A. W. Campbell, from Bailey's Histology.)

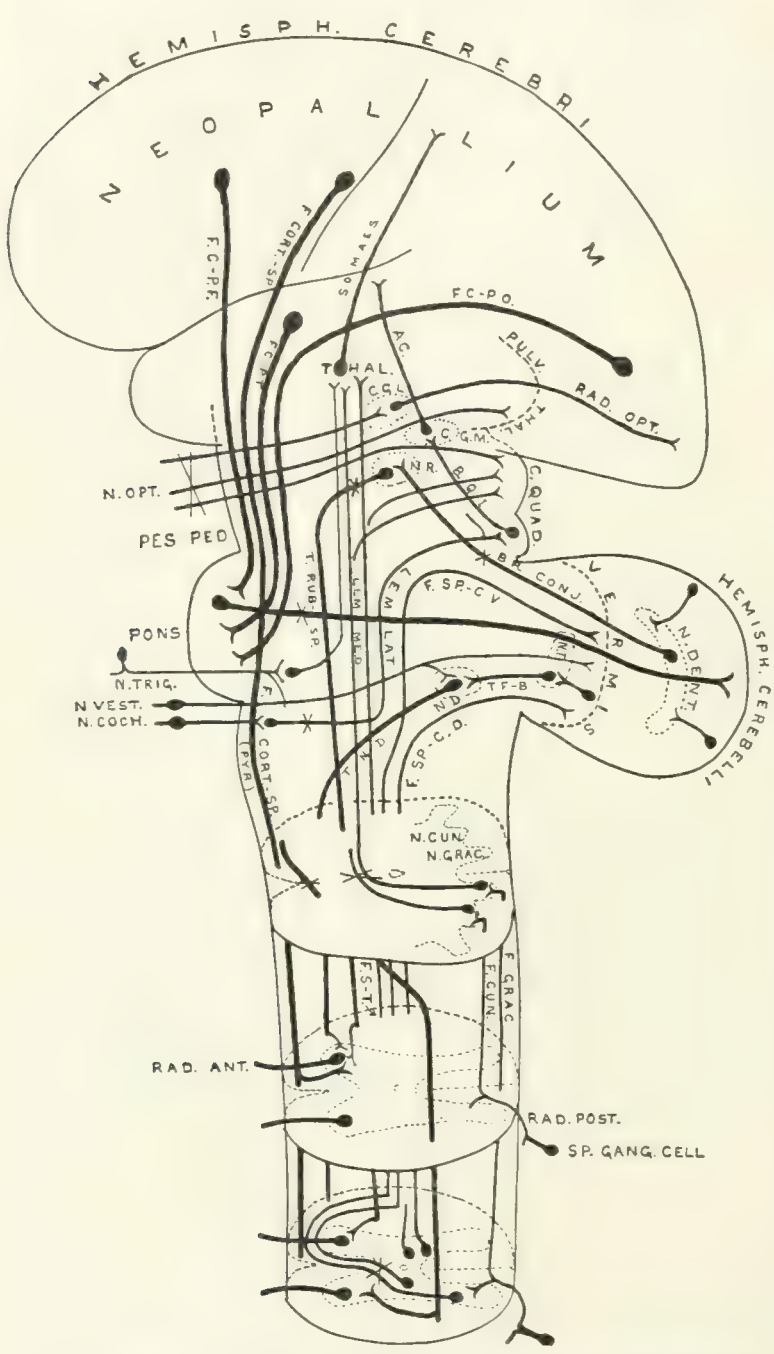

FIG. 989.—Diagram of a Lateral View of the Brain, Illustrating Some of the Principal Connections of the Brain Stem and Neopallium. Each neurone group (nucleus and fasciculus) is indicated by one or several neurones. Decussations of tracts are indicated by an X. *ac.*, Acoustic radiation, from medial geniculate body to temporal lobe of cortex; *b.q.i.*, brachium quadrigeminum inferius, from colliculus inferior to medial geniculate body; *br. conj.*, brachium conjunctivum; *c.g.l.*, corpus geniculatum laterale; *c.g.m.*, corpus geniculatum mediale; *c. quad.*, corpora quadrigemina; *f. cort.-sp.*, fasciculus cerebro-spinalis (pyramidal tract); *f.c.-p.f.*, frontal cortico-pontile fasciculus; *f.c.-p.o.*, occipital cortico-pontile fasciculus; *f.c.-p.t.*, temporal cortico-pontile fasciculus; *f. cun.*, fasciculus cuneatus (Burdachi); *f. grac.*, fasciculus gracilis (Goll); *f. sp.-c. d.*, fasciculus spino-cerebellaris dorsalis (Flechsigi); *f. sp.-c. v.*, fasciculus spino-cerebellaris ventralis (Gowersi); *f.s.-t.*, fasciculus spino-thalamicus (spinal lemniscus); *lem. lat.*, lemniscus lateralis; *lem. med.*, lemniscus medialis; *n. coch.*, nervus cochlearis; *n. cun.*, terminal nucleus of fasciculus cuneatus; *n. d.*, nucleus of Deiters; *n. dent.*, nucleus dentatus; *n. grac.*, terminal nucleus of fasciculus gracilis; *n. opt.*, nervus opticus; *n. r.*, nucleus ruber; *n.t.*, nucleus tecti or nucleus fastigii; *n. trig.*, nervus trigeminus; *n. vest.*, nervus vestibularis, *pes ped.*, pes pedunculi or basis pedunculi; *pulv. thal.*, pulvinar thalami; *pyr.*, pyramid; *rad. ant.*, ventral spinal root; *rad. opt.*, optic radiation from lateral geniculate body to calcarine region of cortex; *rad. post.*, dorsal spinal root; *somæs.*, somæsthetic radiations from thalamus to post-central region of cortex; *sp. gang.*, spinal ganglion; *t.f.-b.*, tractus fastigio-bulbaris; *thal.*, thalamus; *t.n.d.*, tractus vestibulo-spinalis; *t. rub.-sp.*, tractus rubro-spinalis. (After O. S. Strong, from Bailey's Histology.)

a still more highly complex system of suprasegmental centers to serve primarily individually acquired variable associations of the most elaborate kind.

All of the correlation centers of the brain may, therefore, be regarded as derivatives of the formatio reticularis, the higher members of the series being progressively emancipated from the immediate dominance of the peripheral receptors. These higher centers thus receive only such nervous impulses as have been previously coordinated by the lower centers into complexes whose organization is determined by the type of reflex pattern habitually performed by those lower centers. Thus, the cerebral cortex does not receive crude sensory impulses directly from the periphery, but only such afferent impulses as have passed through the basal association centers of the reflex type, there coming into synaptic relation with sensory impulses from other sense organs and being elaborated into adaptive reflex aggregates. These basal centers may discharge directly downward into the motor centers for reflex responses, or they may discharge upward into the cerebral cortex, where a coordination of a higher order is effected and a less immediate type of response follows. The cortical response may reinforce, modify or inhibit the immediate reflex response initiated within the lower center.

In general, the nerve centers of the brain stem serve the reflex and instinctive functions which are determined by the inborn organization, while the cerebral cortex serves the indeterminate associational functions which to a large degree are individually acquired by experience. In the human brain there are important basal centers especially in the thalamus, which have been differentiated within the primordial segmental or intrinsic correlation centers, to serve as a sort of vestibule to the cortex. These centers are especially the lateral and ventral nuclei of the thalamus and the metathalamus. Here the afferent cortical impulses of the lemniscus, optic tracts, etc., are interrupted by synapses before

they pass upward into their respective cortical areas. Thus, the lateral nucleus of the thalamus and the lateral and medial geniculate bodies serve respectively as way-stations between the tactile, the optic and the acoustic nerves, on the one hand, and the cortex. Though a considerable part of the reflex coordination between these important sensory systems is, no doubt, effected in the cortex itself, yet the chief function of the cortex is the establishment of associations of the psychic type.

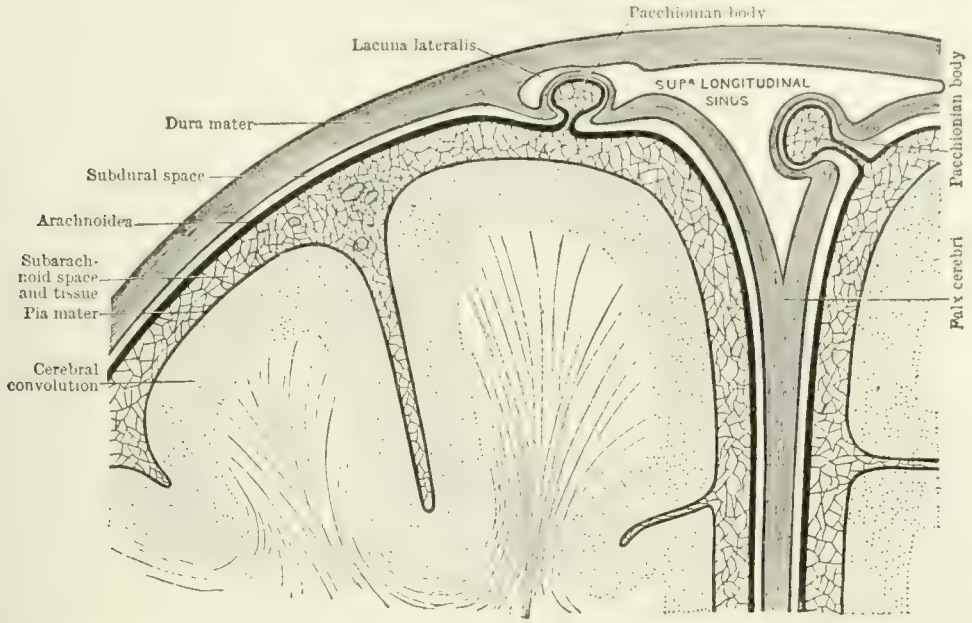

Fig. 990.—Diagram to show the Relations of the Membranes of the Brain to the Cranial Wall and the Cerebral Convolutions, and also of the Pacchionian Bodies to the Superior Longitudinal Sinus and the Lateral Lacunæ. (From Cunningham's Anatomy.)

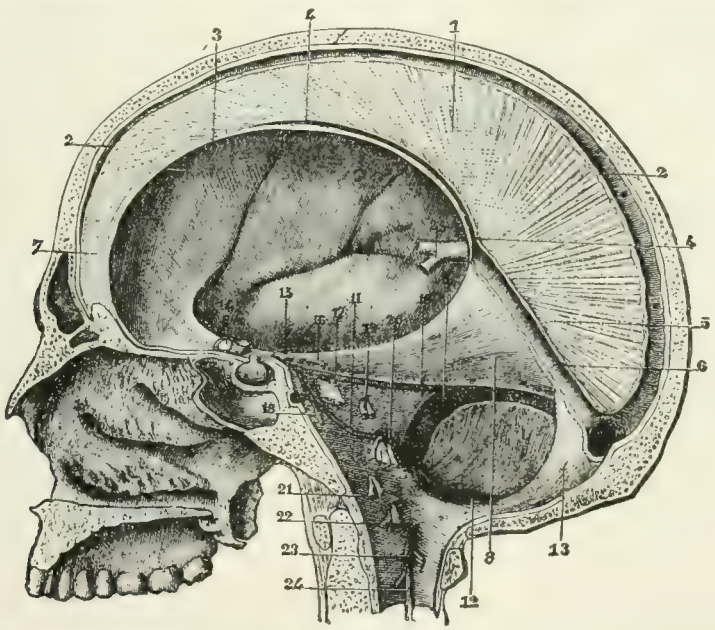

Fig. 991.—Medial Aspect of the Right Half of the Skull, with the Tentorium Cerebelli and Falx Cerebri in Place. 1, Falx; 2, longitudinal sinus; 3, concave margin of falx; 4, facial or inferior longitudinal sinus; 5, base of falx where it joins the tentorium; 6, tentorial sinus or sinus rectus; 7, narrowed anterior end of falx near its attachment to the crista galli; 8, tentorium cerebelli; 9, lateral sinus; 10, superior petrosal sinus; 11, inferior petrosal sinus; 12, posterior occipital sinus; 13, falx cerebelli; 14, optic nerve; 15, oculomotor nerve; 16, trochlearis nerve; 17, trigeminus nerve; 18, abducens nerve; 19, facial and auditory nerves; 20, glossopharyngeal, vagus and accessory nerves; 21, hypoglossal nerve; 22, 23, first and second cervical nerves; 24, ligamentum denticulatum; 25, vein of Galen. (After Sappey.)

The Meninges.—The brain is enveloped by three membranes, from without inward, the dura mater, the arachnoid and the pia mater.

The dura mater of the brain is a dense fibrous

membrane which adheres closely to the skull, for whose bones it serves as internal periosteum, at the same time that it supports the brain. These two functions are performed by separated parts of the membrane in the spinal region, where the bones of the spinal column are provided with separate periosteal coverings, while the spinal cord is enveloped by a distinct cylindrical membranous dura mater, the two being separated by a wide epidural space. The cranial dura mater adheres more or less closely to the skull, with, however, in some places small epidural lymph spaces between. Even within the cranium the dura may be separated in most regions into two layers, and in some places these layers are widely separated to form spaces lined with endothelium, the venous blood sinuses (Figs. 990, 991).

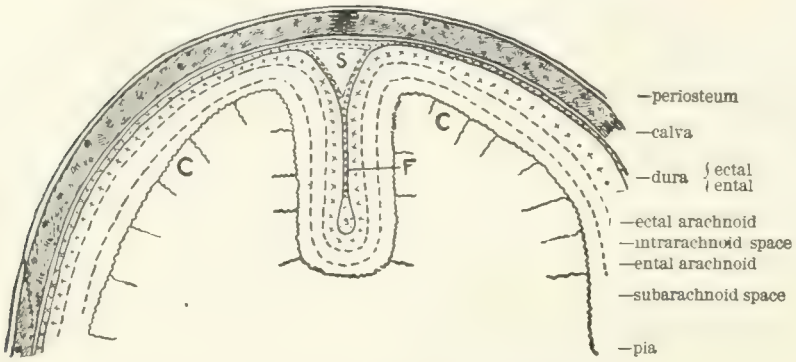

Fig. 992.—Schematic Transverse Section through the Parietal Region of a New-born Babe to Illustrate the Relations of the Meninges to the Cranium and Cerebrum. C.C., Cerebrum; *F*, falx; *S*, longitudinal sinus. (After Langdon.)

From the inner layer of the dura arise several sheets of firm membrane which pass inward between the major divisions of the brain (Fig. 991). The most important of these are the falx cerebri, tentorium cerebelli and falx cerebelli. The falx cerebri descends from the superior longitudinal sinus into the great longitudinal fissure between the two cerebral hemispheres. Along its free border above the corpus callosum runs the inferior longitudinal sinus. The tentorium cerebelli similarly occupies the cleft between the posterior poles of the cerebral hemispheres and the cerebellum. Its posterior attachment to the occipital bone is accompanied by the lateral sinus. The falx cerebelli projects inward from the internal occipital crest below the tentorium between the cerebellar hemispheres.

The arachnoid is an exceedingly delicate membrane which closely follows the inner layer of the dura, from which it is separated by a narrow subdural space. Opinions regarding its relations to the dura differ. The arachnoid is now commonly described as consisting of a single well-defined membrane externally and a mass of very delicate connective-tissue fibers extending across the subarachnoid space between this membrane and the underlying pia mater (Fig. 990). Some of the earlier anatomists, however, taught that the arachnoid is a true closed serous sac, whose parietal layer is more or less closely united with the inner layer of the dura. More recently this view has been revived by Wilder and Langdon, who find that in newborn children a parietal layer of arachnoid can be separated from the dura, but that these membranes are inseparable in the adult except in some regions at the base of the skull. Fig. 992 illustrates this view of the structure of the arachnoid.

The arachnoid, unlike the pia mater, does not follow the irregularities of the cerebral surface. Accordingly, the subarachnoid space is wide in the sulci and practically absent at the summits of the gyri. In some places the subarachnoid space is dilated to form extensive cavities, the cisternæ subarachnoidales. Here the subarachnoid tissue is less abundant. The largest of these is the cisterna magna, lying between the cerebellum and the medulla oblongata (Fig. 993). It communicates with the subarachnoid spaces of the brain and medulla spinalis, and also through the foramen of Magendie, or metapore, with the cavity of the fourth ventricle. The cisterna pontis lies just above the foramen magnum on the ventral side of the oblongata below the pons, and the cisterna basalis farther forward in front of the pons.

Through the medium of the subarachnoid spaces and the metapore there is a free communication for the passage of fluid and the equalization of pressure between the brain ventricles and the fluid "bed" which surrounds the brain on all sides. The materials for constructive metabolism are added to this fluid from the arterial blood supply which is richly supplied to the brain substance and to the pia mater lying below the subarachnoid space. The products of destructive metabolism ultimately leave the cranium chiefly by way of the great venous sinuses. These sinuses not only receive venous blood from the substance of the brain and its meninges by means of the cerebral veins, but there is a special device by which fluid of the subarachnoid spaces may readily diffuse through the brain membranes directly into the large sinuses. This is provided by the granulationes arachnoidales, or Pacchionian bodies. These are small glomeruli or bulbous protrusions of the

Fig. 993.—Medial Section through the Brain Stem and Adjacent Parts, to Illustrate the Cisternæ. The cisterna magna lies between the cerebellum and the roof of the fourth ventricle, the foramen of Magendie (*f.M.*) putting the cavity of the ventricle into communication with that of the cisterna. The cisterna pontis and the cisterna basalis under the ventral surface of the brain stem lie respectively below and above the pons. (After Key and Retzius.)

arachnoid which are pushed outward into the sinuses, especially the superior longitudinal sinus. Each of these is an extension of the subarachnoid space, which carries with it a pouch or globose sac of arachnoidea borne on a contracted pedicle, the whole being thrust into the cavity of the sinus. It carries before it a thin layer of dura mater (Fig. 990). Thus the arachnoid space is separated from the cavity of the sinus only by two very thin membranes and the diffusion of fluid between these cavities is facilitated.

The pia mater is a delicate vascular membrane which follows the contours of the brain very closely and from which the greater part of the internal blood-vessels of the brain are derived.

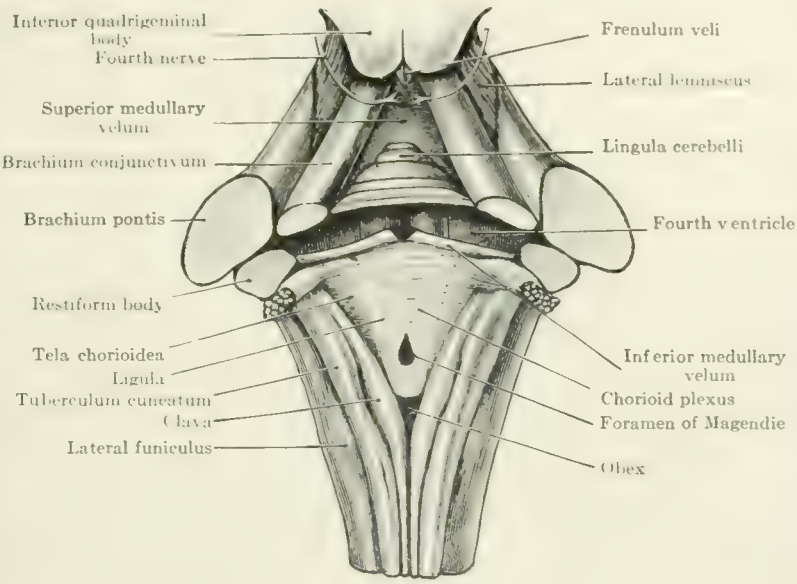

Fig. 994.—Diagram showing the Structures in the roof of the Fourth Ventricle, after the Removal of the Cerebellum. (From Morris's Anatomy, P. Blakiston's Son and Company.)

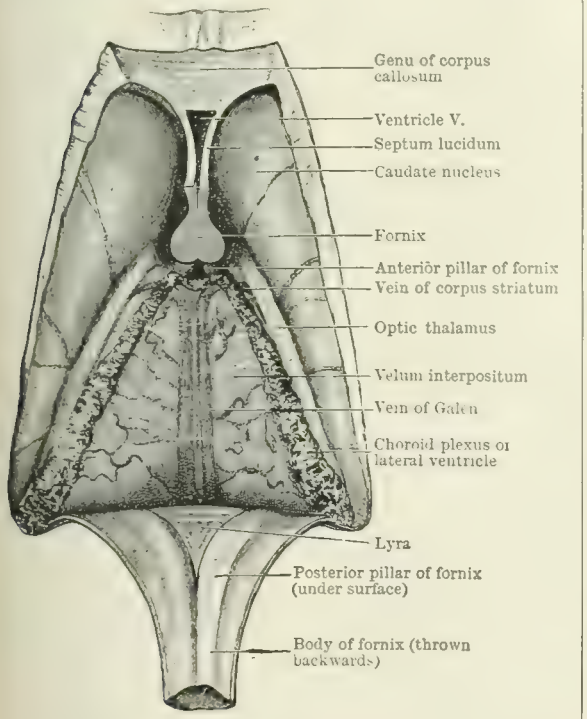

Fig. 995.—Dissection to show the Velum Interpositum and the Parts in Immediate Relation to it. (From Cunningham's Anatomy.)

The pia is closely joined to the membranous parts of the brain wall bounding portions of the fourth, third and lateral ventricles, the two-fold membrane thus formed constituting a tela chorioidea. A portion of each of these membranes is highly vascular, folded and convoluted or crumpled downward into the cavity of the underlying ventricle. These vascular invaginations are the chorioid plexuses.

The tela chorioidea of the fourth ventricle (Fig. 994) is attached to the walls of the ventricle by a thickened border at the tænia ventriculi quarti, termed the ligula. The portion of the ligula which spans the calamus scriptorius is the obex. The transverse fold at the rostral end of the roof of the fourth ventricle where it borders the cerebellum is the inferior medullary velum. The vascular chorioid plexuses of the fourth ventricle are in the form of two parallel masses which in front meet a transverse mass extending outward on each side into the lateral recesses, where they expand to form the "cornucopiæ," which are visible in the intact brain behind the restiform bodies.

The velum interpositum is a triangular fold of pia which lies between the body of the fornix of the

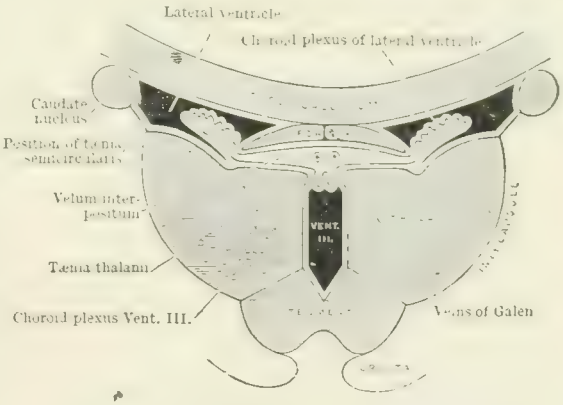

Fig. 996.—Diagrammatic Transverse Section through the Thalamus, to Illustrate the Mode of Attachment of the Chorioid Plexuses of the Third and Lateral Ventricles. (From Cunningham's Anatomy.)

cerebral hemisphere and the thalamus. It is united with the membranous roof of the third ventricle to form the chorioid plexus of the third ventricle, and with the thin non-nervous part of the medial walls of the lateral ventricles to form the chorioid plexuses of the lateral ventricles (Figs. 995, 996). The chorioid plexus of the third ventricle is attached to the walls of the thalamus by the tænia thalami. This plexus is continuous forward at the interventricular

foramen with the chorioid plexuses of the lateral ventricles.

The chorioid plexuses of the lateral ventricles are formed by an invagination of the membranous medial wall of the lateral ventricles (Figs. 968, 971, 996) through the chorioid fissure. One border is attached to the fimbria by the tænia fornicis, the other border is in the embryo attached to the line of contact between thalamus and corpus striatum, *i.e.* to a line bordering the stria terminalis. This is the tænia chorioidea (Fig. 968, *t. ch.*). The portion of this membrane lying between the chorioid fissure and the tænia chorioidea is termed the lamina infrachorioidea (Figs. 967, 968, 977, *l.i.*). In the adult a portion of the lamina infrachorioidea becomes attached to the adjacent wall of the thalamus, so that the line of contact of the membrane with the massive wall of the thalamus (tænia chorioidea) becomes secondarily shifted medialward (cf. Figs. 968 and 996). This band of fusion of the lamina infrachorioidea with the thalamus is known as the lamina affixa. It is visible, but not named, on Fig. 996, where the original line of attachment of the lateral chorioid plexus is indicated by the words, "position of tænia semicircularis."

The function of the chorioid plexuses is not clear. They are distinctly glandular in appearance and in some lower brains show considerable differentiation of structure in different parts. It is probable that they play an important part in the secretion of the cerebrospinal fluid and in maintaining its chemical constitution. The meninges are supplied with nerve fibers which accompany the blood-vessels and are chiefly of vasomotor type, though pain nerves are known to be present also. The substance of the brain itself is entirely insensitive to mechanical irritation.

C. Judson Herrick.

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Brain, Anemia of.—See *Brain, Circulatory Disturbances.*

Brain, Aneurysm of Arteries of.—See *Aneurysm, Internal.*

Brain, Atrophy of the.—A host of conditions is incorporated under this term. By reason of their great variety, it has ceased to be a descriptive term in neurology, save in the broadest sense.

It has been more or less customary to consider ageneses of the brain as forms of cerebral atrophy, but, technically speaking, this is incorrect.

Atrophies of the brain may be localized, or they may be general; may be diffuse, or appear in isolated areas. They may be due to a vast variety of toxemias, or to a number of infections. They may result

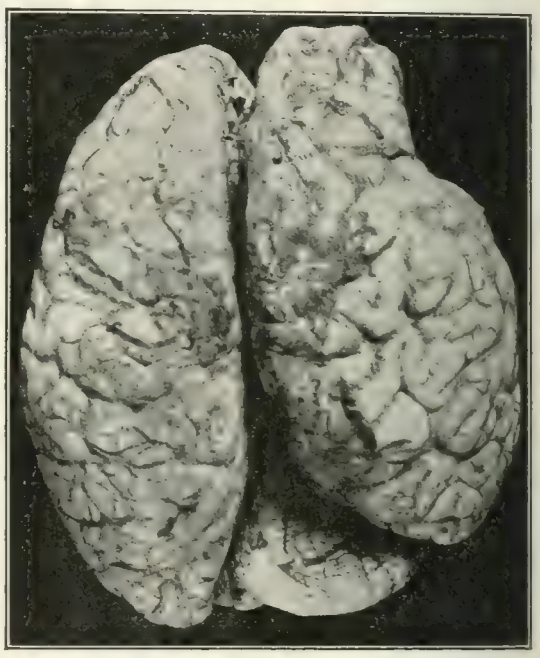

Fig. 997.—Atrophy of One Hemisphere. Old trauma in childhood. Clinically, epileptic convulsions.

from nutritional disturbances, or from old age. They have no settled etiology, no uniform pathology, and no characteristic symptomatology. Therefore, their consideration here is simply to call attention to the various forms of cerebral atrophy that may occur, independent of their relationship. Any scientific presentation of the cerebral atrophies is purely artificial and forced.

Primary agenesis, often called primary atrophy, is seen more particularly in that type of maldevelopment known as microcephalus. This is not a true atrophy, it is simply a failure to develop, a true agenesis. Here the cerebral substance is reduced throughout more or less irregularly, for even under the concept microcephalus one finds an immense amount of variations so far as the distribution of agenesis of the different layers of the cerebrum is concerned.

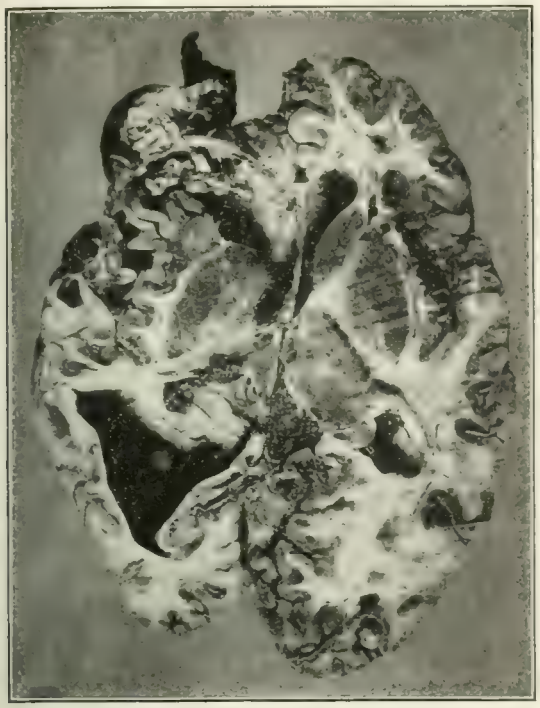

Fig. 998.—Atrophy with Unilateral Hydrocephalus from Old Pistol Wound in Childhood. Clinically epilepsy, hemiplegia, feeble-mindedness. (Munson.)

Fig. 999.—Hydrocephalus with Atrophy of the Entire Pallium. Clinically epileptiform convulsions, feeble-mindness, motor defects. (Craig Colony.)

Microcephalus usually results in various forms of feeble-mindedness, imbecility, or idiocy. Here again one recognizes broad general terms rather than clear-cut description. The characteristic feature in microcephalus is usually the associated diminution in size of the skull, the chambers all being reduced, although occasionally a microcephalic brain may be found within a fairly normal-sized cranium. The weight of the brain itself may often be reduced considerably—even to a few ounces—five to six, the average normal weight being forty to fifty ounces. As a rule, the frontal lobes suffer the most, although there is no definite rule about this. Certain microcephalic individuals are known in whom there is comparatively little loss of intelligence. The actual causes for the lack of development are often unknown. In some

Fig. 1000.—Atrophy of Entire Hemisphere. Clinically hemiplegia (Little's disease). Epileptic convulsions. (Craig Colony.)

syphilis plays a part; in others gross constitutional disturbance of the mother seems to bear some relationship to the agenesis.

Congenital atrophies, as distinct from ageneses, result from a vast variety of pathological processes. Trauma is responsible for a certain number; acute infectious diseases for others; various toxemias for still others. Syphilis is probably one of the most important factors in determining intrauterine cerebral disease, with resulting atrophies, which may be local or general. Poliomyelitis, as an intrauterine disease is also a possibility, and there is reason to believe that acute infections of the mother, other than syphilis, *i.e.* tuberculosis, scarlet fever, measles, etc., may play a very important part in determining cerebral disease of the developing fetus. These various toxemias or infections give rise to cerebral disorders, which in turn destroy, in part or in whole, areas of the cortex, possibly an entire hemisphere, possibly parts of both hemispheres. Thus certain cerebral inflammations

give rise to accumulations of fluid within the ventricles with a formation of hydrocephalus and porencephaly. In these porencephalies the amount of fluid may be excessive, and the cerebral substance reduced almost to a thin sac-like structure. Here the atrophy is very pronounced. This atrophy, due to intracerebral pressure, may be uniformly distributed throughout the cerebral cortex, may involve the midbrain structures, even the motor and sensory pathways. The resulting atrophies will depend largely upon the amount of hydrocephalus, and the clinical pictures will vary from idiocy to imbecility, to high-grade feeble-mindedness, epilepsies, etc.

Encephalitis, due to certain of the infections mentioned, is a not infrequent cause for more or less localized forms of cerebral atrophy. Clinically they show themselves in later life as various types of feeble-mindedness or idiocy; in epileptiform convulsions, or possibly congenital defects of speech, in forms of monoplegia, diplegia, pseudobulbar palsy, etc. Here the atrophy of the brain structures may be more or less localized, and is conditioned by acute inflammatory processes in the cerebral substance. Certain forms of pachymeningitis, or hemorrhage from traumatism, occur in later intrauterine life, or at the time of birth. Here localized pressure may result in localized atrophies, giving rise to a variety of clinical pictures, among which will be found various forms of epilepsies, of feeble-mindedness, monoplegias, diplegias, so-called Little's disease, hemiplegias, athetoses, tremors, speech defects, aphasias, congenital blindness, congenital deafness, etc., etc.

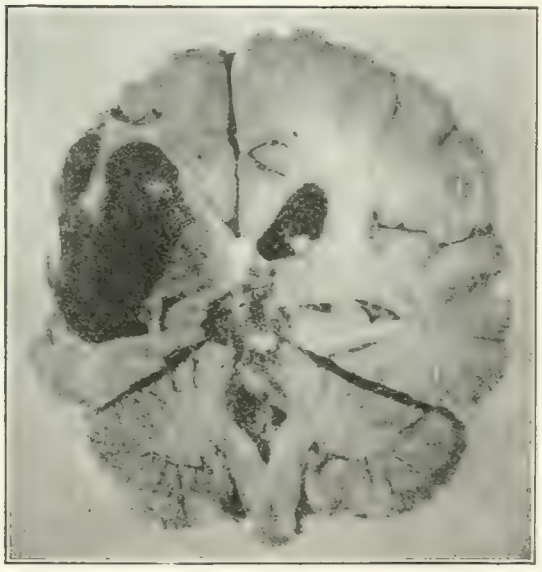

Fig. 1001.—Unilateral Dilatation of Ventricle. Atrophy of pallium. Clinically hemiplegia, psychic defect. Epileptic convulsions. (Craig Colony.)

Here the atrophies also escape all attempts at systematic classification. They are an extremely heterogenous group.

Atrophies Found in the Adult.—Here again no systematic presentation is possible. The brain of a chronic alcoholic may be found atrophied as the result of his alcoholism. Chronic lead poisoning may have the same result. In patients suffering from Addison's disease localized atrophies are found. Atrophies also result from encephalitis, meningoencephalitis, tuberculosis from tumors, from long-wasting diseases, from senility. A very characteristic and widespread atrophy is present in general paresis, one of the forms of cerebral syphilis. Irregular and diffuse atrophies are very characteristically found in many forms of dementia præcox. These various types of atrophy will show considerable variation as to involvement of particular layers, or as to distribution. Thus the atrophies in general paresis are extremely variable. Although the frontal lobes seem to bear the brunt of the disturbance in the majority of cases, yet there are distinctly localized atrophies in paresis in which the occipital, or the temporal, or the parietal lobes are more involved than others. In amyotrophic lateral sclerosis there is a distinct atrophy for instance of the

Fig. 1002.—Atrophy of Cerebellum in General Paresis.

motor areas, more or less limited to the layer of Betz cells. In dementia præcox irregular atrophies are extremely frequent and widespread. Here deeper layers of the cortex show definite atrophy. The atrophy of senility, often accompanied by the mental picture of a senile psychosis, also offers considerable variation. That special form of presenile psychosis, known as Alzheimer's disease shows a number of extremely characteristic alterations in the cortex, with basket-like areas of degeneration and cellular atrophy.

In certain atrophies the ganglion cells suffer, in others the neuroglia tissues, in others the fibers. In fact a multitude of changes are found when one comes to cite the various atrophies and scleroses of the cerebral cortex.

Properly speaking there is no such thing as a prognosis of atrophy of the brain, since there is no such entity, nor can one speak of a diagnosis, and still less of a treatment. The mode of looking at the various atrophies here presented prevents any such generalization, and therefore one is referred to the various disease processes which are mentioned as accompanied by or causative of the cerebral atrophies.

Smith Ely Jelliffe.

Brain, Cerebellar Disease.—See *Cerebellum Disorders of the.*

Brain, Circulation in the.—All the larger intracranial vessels and most of their easily visible branches lie in the enveloping membranes—dura, pia, and their processes. Over the convexity only minute branches enter or leave the brain proper. The largest arterial twigs directly entering the cerebrum are those of the (basal) pre- and postperforated spaces. The largest venous rootlets directly from the organ are the corresponding perforants and some in the cœles. Hence the vessels of the meninges have to be included in any account of the encephalic circulation; and the vascular distribution—especially the arterial—can be best mapped out on the surface. In this article the simplified terms of Wilder, as well as those of the BNA, will be employed. These are extended also to the veins, sinuses, and so-called meningeal vessels. As these last lie wholly in one of the membranes, the dura, the general term *meningeal* does not accurately define them; for this the unequivocal *dural* is substituted.

Arteries.

The encranial arteries present two distinct systems of vessels:

I. The dural, commonly called meningeal.

II. The intrinsic, or those of the brain proper.

These latter do not anastomose with any other arteries. Rarely there are marked exceptions to this rule, and perhaps oftener slight inosculations about the sella turcica.

Heubner (1874), from injections in adults, says: "The territories of the medidural and of the cerebral arteries must be considered as absolutely independent of one another." Langer (1877), speaking of infantile and young subjects, states: (*a*) that one or two dural branches of the precerebral anastomose in the falx with terminal twigs of the dural artery; (*b*) also that pial branches of the precerebral may reach minute dural arteries accompanying the supercerebral veins as they spring over to the dura near the longitudinal sinus.

I. The Dural vessels (*meningeæ*) ramify in the exterior of the dura. In a general way it is true that the pre-, medi-, and postdural arteries are branches respectively of the internal and external carotid and vertebral arteries. These various branches interanastomose freely, so that dural infarction does not occur. They are distributed not simply to the dura, but also to the diploic cranial bones; small twigs may also pass to extracranial parts.

1. *The Branches from the External Carotid* supply the middle belt, and, in fact, nearly the whole of the dura. They are:

(1) The *Medidural*, the largest and most constant of all the dural arteries, arising from the internal maxillary and entering through the spinous foramen. Its branches pass up the divergent sulci meningei (for arteries and accompanying veins) of the lateral cranial wall, connecting at the top with those from the opposite side. Of its two main divisions, the larger anterior is often for a short distance arched over to a canal.

The furrows of the medidural artery on the entocranial wall deepen with years, and in old age the artery sinks quite into them. It has two primary branches, a larger cephalic and a caudal, the former again soon (at the sphenoidal angle of the parietal bone) separating into two secondary rami. The anterior ramus runs up behind the coronal suture, though a little more obliquely, being, according to Marchant, pretty constantly from 0 to 13 millimeters (averaging 5 to 6 millimeters) away at the foot of the suture, about 1 centimeter at its middle, and 15 millimeters at its dorsal part. The second ramus starts on the entotemporal surface 4 centimeters behind the pterion, on an average. At its middle, on the entoparietal surface, it averages 54 millimeters behind the coronal suture. Farther dorsad, the distance is very variable, 30 millimeters more or less.

The primitive caudal branch leaves the temporal squama 58 millimeters behind the pterion, then goes toward, and becomes parallel with, the lambdoidal suture.

The relations of these vessels to the subjacent cortex, important clinically, Duchaine sums up thus: (1) The cephalic branch runs up opposite the frontal lobe some centimeters before the central fissure, rather nearer the coronal suture. (2) The midramus starts almost opposite the fissure, then runs up some centimeters behind it. (3) The caudal branch is always a centimeter or more distant from the fissure, and is still farther separated above.

Besides many minute branches to the sinus walls, outgoing nerves, and orbit (*vide infra*), it may send to, or receive from, the deep external temporal region minute rami perforating the interposed wall; in young subjects (Hyrtl) considerable branches may pass through the anterior fontanelle and the sagittal suture to the soft cranial coverings.

(2) The *parvidural*, an inconstant accessory medidural, arising close to the latter, or even directly from it, and entering by the oval foramen. It goes to the Gasserian ganglion and adjacent dura.

(3) The *Mastoid* branch of the occipital (or external carotid, fifteen in one hundred and twenty times, Wyeth, 1878), entering by the mastoid foramen, within which it always sends a branch to the diploë. It is small, variable, and destined for the wall of the lateral sinus and adjacent dura. Here again a reverse course has been observed, where the postauricular arose from a dural artery by emerging through a foramen in the mastoid (Bankart).

(4) *Supradural* branch or *Ramus parietalis*, also from the occipital, accompanying the emissary through the parietal foramen. It is usually insignificant, and often absent.

(5) The *Subdural* branches are very small and variable. They include twigs from the ascending pharyngeal, occipital, and stylomastoid arteries, enter by the pre- and postlacerated, precondyloid, and stylomastoid foramina, and partly supply the dura of the posterior fossa and basilar sinuses.

2. *Branches from the Internal Carotid.*—(1) The cavernous carotid yields several small rami to the sinus wall, the pituitary body, Gasserian ganglion, and dura about the sella turcica. These are variously styled *receptacular* and *rayed arteries*, even predural in case of any prominent single branch. Their field of distribution and that of the parvidural are evidently complementary.

(2) The *Predural* usually refers to the one or more slight branches of the ethmoidal arteries, supplying the adjacent dura of the precranial fossa.

3. *Branch from the Vertebral.*—The *Postdural* artery arises opposite or just below the occipital foramen, passes with the vertebral into the cranial cavity, and supplies the dura of the postcranial fossa, especially the posterior portions as the cerebellar falx, etc.

The only anastomoses of special interest, between dural and extradural arteries, are with those of the orbit. Such connections always exist. Often a medidural branch enters, through either the sphenoidal foramen or some special opening, and supplies the external wall, even substituting partly or wholly the lacrymal artery, or a branch of the lacrymal may take the reverse course. Very rarely the medidural arises directly from the ophthalmic (Zuckerkandl, four cases, Hulston, one), and then passes by the sphenoidal fissure to its usual distribution. This possible origin should be borne in mind in the operation of tying the medidural at the base of the skull.

II. Intrinsic Arteries (or those of the pia and brain substance).—In removing the brain from the skull we sever at its base the four arteries which suffice

Intrinsic Arteries of the Brain.

Common Latin names.	Proposed names.	English paronyms.	B. N. A.
Vertebralis	Vertebralis	Vertebral	Vertebralis.
Basilaris (az.)	Basilaris	Basilar	Basilaris.
Cerebellaris superior	Precerebellaris	Precerebellar	Cerebelli superior.
Cerebellaris anterior	Medicerebellaris	Medicerebellar	
Cerebellaris inferior	Postcerebellaris	Postcerebellar	Cerebelli posterior.
Cerebralis anterior	Precerebralis.	Precerebral.	Cerebri anterior.
Corporis callosi			
Cerebralis media	Medicerebralis	Medicerebral	Cerebri media.
Fossæ Sylvii			
Profunda cerebri	Postcerebralis	Postcerebral	Cerebri posterior.
Cerebralis posterior	Precommunicans	Precommunicant	Communicans anterior.
Communicans anterior (*az.*)	Postcommunicans	Postcommunicant	Communicans posterior.
Communicans posterior	Prechoroidea	Prechoroid	Chorioidea.
Choroidea anterior	Postchoroidea	Postchoroid	
Choroidea posterior	Preperforantes	Preperforants.	
Perforantes anteriores	Postperforantes.	Postperforants.	
Perforantes posteriores			
Termatica (*az.*)	Termatica	Thermatic.	
Cerebralis ant. media.			

Dural Arteries.

Meningea	Duralis	Dural	Meningea.
Meningea anterior.	Preduralis	Predural	Meningea anterior.
Meningea media	Mediduralis	Medidural	Meningea media.
Meningea parva	Parviduralis	Parvidural	Ramus meningeus accessorius.
Meningea posterior.	Postduralis	Postdural	Meningea posterior.
Meningea inferior	Subduralis	Subdural.	

Sinuses.

Longitudinalis superior (*az.*)	Longitudinalis.	Longitudinal.	Sagittalis superior
Longitudinalis inferior (*az.*)	Falcialis	Falcial	Sagittalis inferior.
Torcular Herophili (*az.*)	Torcular.	Torcular.	Confluens sinuum.
Confluens sinuum			
Sphenoparietalis	Sphenoidalis	Sphenoidal	Sphenoparietalis.
Ale parvæ			
Petrosus superior	Superpetrosus	Superpetrous	Petrosus superior.
Petrosus inferior	Subpetrosus	Subpetrous	Petrosus inferior.
Petrosus anterior	Prepetrosus	Prepetrous.	
Rectus (*az.*)	Tentorii	Tentorial	Rectus.
Lacunæ laterales sinuum	Lacunæ parasinuales	Parasinual* spaces.	

Intrinsic Veins of the Brain.

Cerebri superior	Supercerebralis	Supercerebral	Cerebri superior.
Cerebri anterior	Precerebralis	Precerebral.	
Callosi anterior externa			
Cerebri media	Medicerebralis	Medicerebral	Cerebri media.
Fossæ Sylvii	Sylvii	Sylvian.	
Basilaris Rosenthali	Subcerebralis	Subcerebral	Basalis (Rosenthali).
Cerebri inferior s. ascendens			
Occipitalis lateralis	Postcerebralis	Postcerebral.	
Cerebralis lateralis et inferioris			
Occipitalis interna	Suboccipitalis	Suboccipital.	
Cerebri posterior inferior			
Callosi posterior externa	Callosalis	Callosal.	
Magna Galeni	Galeni	Galen's	Cerebri magna (Galeni).
Cerebri interna communis			
Cerebri interna s. intima s. profunda	Velaris	Velar	Cerebri interna.
Right and left vein of Galen			
Corporis striati	Tænialis	Tenial.	
Lateralis ventriculi			
Cornu anterioris	Precornualis	Precornual.	
Septi lucidi	Paraseptalis	Paraseptal	Septi pellucidi.
Antr.-ventriculi			
Cornu posterioris	Postcornualis	Postcornual.	
Choroidea	Medicornualis	Medicornual	Chorioidea.
Medullares superiores	Superalbales	Superalbals.	
Rami corporis striati	Striatales	Striatal.	
Rami thalami optici	Thalamici	Thalamic.	
Ramus thalami optici profundus (Rosenthal)	Thalamocruralis	Thalamocrural.	
Pedunculi cerebri			
Azygos conarii	Conarialis	Conarial.	
Cerebelli sup. media	Supercerebellaris	Supercerebellar	Cerebelli superior.
Cerebelli sup. lateralis	Paracerebellaris	Paracerebellar	
Cerebelli inferior	Subcerebellaris	Subcerebellar	Cerebelli inferior.

Dural Veins.

Duræ matris cerebri	Duralis	Dural	Meningeæ.
Meningea			
Meningea media	Mediduralis	Medidural	Meningea media.
Ophthalmomeningea.	Ophthalmoduralis	Ophthalmodural	Ophthalmomeningea.

* The form parasinual was kindly suggested and approved by Prof. B. I. Wheeler, the comparative philologist.

for its entire blood supply. These are, anteriorly, the two carotids entering through the carotid foramen and canal; posteriorly, the two vertebrals entering beside the foramen magnum. By means of communicating branches at the base of the brain—the vertebrals having first united, and their common basilar trunk having divided into the two postcerebrals—the primary vessels combine to form the circle of Willis. From this practically all and only the *cerebral* arteries emanate. Previously, however, several branches are given off by the vertebrals and basilar; while the carotid yields only the ophthalmic. The latter is said always to originate before any of the cerebral branches, and some millimeters before the bifurcation of the cerebral carotid.

The Vertebrals and Basilar supply in their course the organs of the posterior fossa, viz., cerebellum, pons, oblongata, and their adnexa. In approaching the distal border of the pons the vertebrals unite to form the mesal basilar. This is occasionally divided within by a septum, or separates into two vessels which soon reunite. The basilar lies in the median sulcus of the pons, directly on the basilar process of the occipital bone; opposite the central border of the pons it ends in the two postcerebrals. Only occasional variations are attributed to the vertebrals: (1) absence of one, the existing vessel being joined by a branch from the opposite carotid; (2) both may join the basilar on the same side; (3) or one may be represented by two or three branches before entering the formation of the basilar trunk.

The lateral branches are:

1. *Postcerebellar*, the largest offshoot of the vertebral. It passes around the oblongata, beside the pneumogastric nerve, to supply the extremity of the cerebellar lobe as far as the median line, the subvermis and adjacent surface, and the plexus of the metepicele.

2. *Recurrent spinal twigs*, also from the vertebral, are given as follows by Kadyi: Immediately after the vertebrals traverse the dura there arises from each a one-millimeter-thick branch (dorsomyelic), which, after giving up twigs to the restiform body, descends along the dorsal border of the lateral columns of the cord. This is homologous with other branches entering by the dorsal nerve roots. Sometimes this arises from the vertebral in common with the postcerebellar.

Near the union of the vertebral to the basilar there arises—usually one on each side, though unequal—the myelic branch for the ventromyel. These two, however, either soon, or oftener after entering the spinal canal, combine to form the azygoid ventromyelic (anterior spinal) artery. They are thus continuous and homologous with the other myelic arterioles coming in along the ventral nerve roots.

A full consideration of the minute details of the arterial distribution in the oblongata is given by Adamkiewicz (*vide* Plate XVII.). These vessels come wholly from the upper (intracranial) part of the vertebrals as they cross the ventral surface of the oblongata.

The main facts regarding the three classes of secondary or nutrient arterioles (external or surface vessels) he accepts from Duret: 1. The radicals, direct from the vertebrals, supply the outgoing nerve roots (facial, acoustic, glossopharyngeal, vagus, accessorius, and hypoglossus). 2. The nuclears, at right angles from the one or two dorsomyelics in an extent of three to four centimeters. These penetrate the median fissure, at the bottom of which they form a kind of sagittal leader, and end beneath the floor of the metepicele (fourth ventricle). 3. Arteries for the other portions of the oblongata (olivary bodies, pyramids, corpora restiformia), in part at least from the myelics.

Moreover, on the oblongatal surface is a rich network of vessels. The ventromyelics opposite the oblongata give off a multitude of twigs that take a very sinuous course and soon settle into the furrows. For the dorsal surface of the oblongata there is no external supply until below the calamus—upper end of myel. Its source is the dorsomyelics. These latter, at the first cervical roots, turn caudad between the accessory nerve roots (nearer the dorsal), and when at the level of the fourth or fifth cervical roots they end by also anastomosing with vessels of lower origin.

From the middle portion of the vertebrals, between the ventro- and dorsomyelics (anterior and posterior spinals) arise the largest branches (subcerebellars), but these dodge the oblongata and are wholly for the cerebellum.

Topographically, Adamkiewicz distinguishes three sets of finer or nutrient arterioles (internal or substantial vessels) after the manner of the myelic supply.

(1) Ventrofissurals, relatively large, dividing in the ventral commissure into two branches, one to each side for the corresponding ventromesal cinerea. In the oblongata these supply principally the pyramidal tracts and decussation, lemniscus, interolivary tract, raphé, and the following nuclei—gray dorsal columna, n. pyramidalis, n. arciformis, oliva, and hypoglossus.

(2) Dorsofissurals, of course only caudad of the calamus. These divide at the dorsal commissure into two border vessels, and are for the substance of the dorsal columns, nucleus gracilis, accessorius center, and casually the hypoglossus.

(3) Coronal, radial, or lateral system. These are very numerous, penetrate the alba from all sides (excepting of course the metepicele, or fourth ventricle, and in part reach the sudjacent cinerea to help form then its mass of capillaries. A subclass here—nuclear arteries—consists of six to eight relatively large twigs entering the angulus restiformis olivaris and running parallel toward the middle of the floor of the fourth ventricle, to supply principally the centers for glossopharyngeus, vagus, hypoglossus, and acusticus. The following parts receive these radial or lateral affluents—the ventral columns, lateral nuclei, lateral cornua, caput of substantia gelatinosa, nuclei cuneati gracilis, arciformis et pyramidalis, and the oliva itself.

3. *Medicerebellar*, usually from the basilar trunk. This passes along the middle cerebellar crus to the preventrad surface of the respective cerebellar hemisphere, including the flocculus.

4. *Transverse* branches, three or four in number. These are parallel and accessory to the preceding.

5. *Auditiva Interna.*—Starts like the last, but passes to the internal auditory meatus and structures of the inner ear.

6. *Ponticular* branches.—These immediately enter the pons perpendicularly, and supply its substance. They represent true terminal arteries (Heubner), quite comparable to the perforants of the cerebrum. From the importance of the tracts supplied they have likewise great interest to the pathologist.

7. *Supercerebellar.*—This starts near the end of the basilar, passes outward along the front border of the pons, winds around the crus cerebri near the optic lobes, and is distributed to the supervermis and general dorsal surface of the cerebellum. It also supplies the postoptic arteries.

The basilar branches all emanate at practically a right angle to the mother trunk. Those going to the surface anastomose much more freely than do the cerebral arteries. Accordingly Heubner found the pia districts of single arteries much less definite over the cerebellum than over the cerebrum. Moreover, the branches of the two sides communicate dorsad across the median line; this is explained by the development of the cerebellum from a single median vesicle. The only communication between this system of vessels and the cerebral—except through the basilar trunk—is by small branches of the precerebellars and postcerebrals across the crura cerebri.

Circle of Willis.—The carotid ends at the outer angle of the chiasma in two main branches, the pre- and medicerebral arteries. At about one centimeter in front of the chiasm the two precerebrals are connected by the precommunicant. From either the medicerebral or the carotid passes the postcommunicant to the corresponding postcerebral. Hence the circle (or polygon) of Willis is made up by one precommunicant, two precerebrals, two medicerebrals (or two carotids), two postcommunicants, and two postcerebrals. This is the classical arrangement; from it, however, there are frequent and important deviations. Windle found that it held in only 76, or, overlooking any disproportion in the postcommunicants, in 119 out of 200 cases. Only in the apes do the vertebrals nearly equal the carotids. In man, Ehrmann, from 157 measurements, found that very constantly the basilar trunk was equal to one carotid (*i.e.* furnished one-third of the brain supply). The communicants are not simply to reestablish a circulation in case of obliteration, but they normally act to equalize pressure in the local vessels. When this circle is complete and of normal structure, an adequate collateral circulation is established after occlusion of any one part. From this circle and the first few centimeters of its branches originate a multitude of arterioles passing to the basal ganglia and adjacent structures.

Dercum offers "A Collection of Anomalies of the Circle of Willis" (*Journal of Nervous and Mental Diseases*, 1889, January), and J. H. Lloyd (*Ibid.*, 1890, p. 225) gives such a case of a type described by Duret (right vertebral absent, both precerebrals from left carotid, etc.). St. John Bullen (*Journal of Mental Science*, 1890, January, p. 33) bases the following statements on the examination of 1,565 brains (from the insane), but holds statistics too uncertain. Arterial variations occur much oftener in general paralytics than in those dying of other forms—this applying equally to all segments of the circle of Willis.

The components of this circle and their branches:

The Precommunicant.—This is a transverse branch beneath the rostrum, from 1 to 2 millimeters in size, connecting the two precerebrals, and forming the anterior side of the circle. Windle found it normal in 159, double in 14, incompletely so (forked at one extremity) in 6, triple in 1, absent in 8, and associated with union of the precerebrals in 2. Wilder notes the latter condition in 6 out of 7 cases, and Starr in 2 of 14. Duret says that when double one is of normal size, the other very small. Its place is sometimes supplied by a fasciculus of small twigs. The precommunicant, Bullen finds, may be absent, or merely rudimentary, or double. Its branches—more numerous when the communicant is unusually long—are:

1. The *Termatica.*—A mesal vessel at its origin. Wilder found this present in all of seven brains examined. "It usually divides soon into a right and left portion, which supply respectively the cinerea forming the surface of the triangular area ventrad of the genu and rostrum, and then extend around the genu to the dorsal aspect of the callosum." Windle notes it in nine of his cases. It passed along the longitudinal fissure for two-thirds of the length of the callosum, and divided into branches supplying the opposed surfaces of the hemispheres. When the communicant is wanting, this vessel may start from the junction of the precerebrals.

2. Small retrograde rami to the lamina of the chiasm.

3. Arterioles which plunge into the callosal rostrum, and very often one or two considerable branches completely perforating the rostrum and ramifying on the crura of the fornix, the anterior commissure, and the septum.

The Precerebral (*vide* Plate XIX. and Fig. 1003, 3).—This originates at almost a right angle from the carotid. Often the artery of one side is larger than, and partly substitutes, that of the other side. Windle found it normal in 181 of 200 cases. In 2 the right was absent, its place being partly supplied in one by twigs from the right medicerebral, in the other by a small branch from the carotid. In 1 the right was double the size of the left; in 1 the two united to a single trunk; and in 8 they united for a short distance, six times replacing and twice accompanying the precommunicant. Either precerebral may, according to Bullen, (1) be replaced by two small trunks, or (2) be absent, its region being supplied by branches of the opposite artery.

The short oblique portion, dorsad of the optic nerve, between carotid and precommunicant, represents part

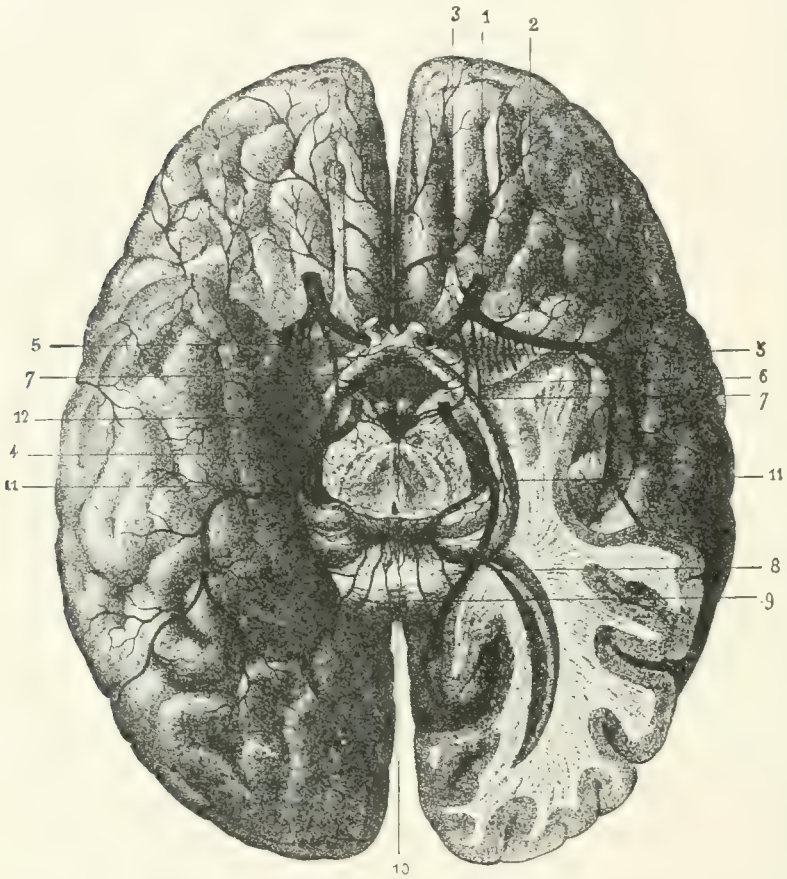

Fig. 1003.—Arteries of the Base. (After Duret.) 1, Carotid; 2, medicerebral; 3, precerebral; 4, postcerebral; 5, preperforants (striate arteries); 6, prechoroid; 7, postcommunicants; 8, postchoroid; 9, medichoroid; 10, callosals (termination of precerebrals); 11, medioptics; 12, prethalamic (postperforants). The carotids are drawn frontad to show the preperforants. The left temporal lobe is cut away, exposing the medicerebral trunk at the bottom of the Sylvian fissure, and also its branches crossing the insula.

EXPLANATION OF PLATE XVII.

EXPLANATION OF PLATE XVII.

ARTERIAL SUPPLY OF OBLONGATA (FROM ADAMKIEWICZ). ENLARGED SIX DIAMETERS.

FIG. 1.—At Decussation of Pyramids.

Hs, Dorsal Column.
Ng, Nucleus gracilis.
Nc, Nucleus cuneatus.
Sgc, Substantia gelatinosa centralis.
Ccp, Caput cornu posterioris (aut tuberculum Rolando).
XII, Root of hypoglossus.
Vr, Remnant of ventral column.
Prk. Decussation eminence.
Py, Pyramid.
g, Boundary between Py and Vr.
S, Arteria sulci.
Sa, A. sulci (at deeper layers).
Acc, Aa. centrales cornuum anteriorum.
Aca, Aa. cornu anterioris.
Anl, A. nuclei lateralis.
As R, A. tuberculi Rolando.
Anc, A. nuclei cuneati.
Ang, Aa. nuclei gracilis.
F. A. fissuræ.

FIG. 2.—Opposite Middle of Metepicœle.

H, Hypoglossus nucleus.
Va, Post. vagus nucleus.
Po, Ponticulus (velum medullare posticum).
Gl, Glossopharyngeus nucleus.
Ac, Acusticus nucleus.
Lb, Longitudinal bundle.
(Krause's respiratory fasciculus.)
Cr, Corpus restiforme.
X, Ant. vagus nucleus.
IX, Root of glossopharyngeus.
Aro, Angulus restiformio-olivaris.
O, Oliva.
No, Nucleus pyramidalis.
Ozs, Interolivary tract.
R, Raphé.
Py, Pyramid.
Na, Nucleus arciformis.
S, Arteria sulci.
Sce. Affluents to external nest-like capillary coils, from sulcus artery.
Sci, Affluents to inner same.
Aoli, Sublateral olivary artery.
Aso, Olivary ramus from sulcus artery.
Aoli, Subolivary arteries.
Aolm, Medilateral olivary artery.
Aols, Super-olivary artery.
An, Arteries of the nuclei (glossopharyngeus, vagus, hypoglossus).
Vn, Nuclear vessels (glossopharyngeus, acusticus).
F, Arteria fissuræ.

FIG. 3.—Longitudinal Section through Olivary Body.

O, Oliva.
Br, Pons.
Aoli, Aa. olivæ laterales inferiores.
An, Aa. nucleariæ.

Arterial Supply of Oblongata (from Adamkiewicz.)

of the circle of Willis. This portion may give off the following branches: 1. Arterioles to the optic nerve of the same side. 2. Lateral arterioles to the neighboring convolution and the callosal rostrum. 3. When, from premature division of the carotid, the precerebral goes over a long course, it much oftener gives large twigs to the caudate (*preperforantes*). Duret says that these branches take one of two courses. In one they penetrate almost within the expansion of the olfactory nerve, perforate the callosum at its junction with the lower part of the caudate head, and divide into five or six almost subependymal ramifications not extending beyond the first two centimeters of the caudate. In the other, one or two arterioles, of about one millimeter diameter, follow a retrograde course of three to four centimeters to the preperforated space beneath the caudate, to which latter exclusively they are distributed.

From the precommunicants on, the precerebrals run side by side around the genu and caudad at the bottom of the longitudinal fissure. After giving off the first few branches the main trunk may divide into three branches, as stated by Duret, whose description is largely followed; or several successive branches are given off, as in the accompanying plate. Together, they supply the inner two-thirds of the ventral surface of the frontal lobe, the anterior four-fifths of the opposed surface of the hemispheres, the callosum (largely), and a portion of the convexity.

1. *Subfrontal* twigs, to the olfactory groove and region as far as subfrontal sulcus. 2. *Prefrontal* branch, to mesal surface of superfrontal and convex surface of superfrontal and part of medifrontal convolutions. 3. *Medifrontal* branch, to the callosal convolution, and paracentral lobule. After doubling the crest of the hemisphere it terminates about the dorsal extremity of the central fissure. 4. *Postfrontal* branch, to precuneus and the adjacent portion of the convexity, nearly or quite reaching the occipital fissure. 5. *Callosal* artery. This may pass around the splenium to terminate in the pineal gland, and even posterior commissure. It goes to the callosal convolution and vault, perforating the latter and ramifying over the whole extent of the roof of the paraceles.

The Cerebral Carotid (Fig. 1003, 1).—As a rule the postcommunicant is a direct branch of the carotid, though it often starts from the medicerebral. In the former case the carotid, from this branch to its termination at the commencement of the Sylvian fissure in the pre- and medicerebrals, forms part of the circle of Willis. In this short course a few lateral branches are given off:

1. Arterioles to the external angle of the chiasm. Either these or the *chiasmic* arterioles from the precerebral supply minute twigs to the first portion of the optic nerve. 2. Frequently, one or more of the *perforantes* to the caudate. 3. *Prechoroid* (Fig. 1003, 6). This may come from the medicerebral, or even from the postcommunicant; in any case its origin is peripheral to that of the last named. It is directed obliquely caudad along the outer side of the optic tract to attain the choroid plexus in the lateral horn (through the extremity of the transverse or Bichat's fissure). It gives off: (*a*) internal and slightly recurrent branches to the optic tract; (*b*) internal branches for the central part of the outer aspect of the crus cerebri; (*c*) external branches to the uncus (a terminal arteriole, Heubner); (*d*) extremely fine twigs to the two-thirds of the choroid plexus that it is stated to traverse.

In general, Kolisko's work corroborates that of Heubner. In a large number of examinations this vessel was never absent. It has a pretty constant diameter of 0.5 millimeter. In the fetus it is relatively very large. In animals (dogs, cats, rabbits) it was regularly present, but arose from the Sylvian. The branch to the uncus was always present, but has free anastomosis in the pia. The branches in plexus and tela also anastomose freely with others near; but those to the brain substance are terminal.

The prechoroid supplies the following parts: The posterior arm of the internal capsule, with the lamina medullaris externa of the thalamus to the level of the upper angle of the midlenticular segment—usually only the posterior two-thirds; the white substance back of the internal capsule as far as the roof of the medicornu; the inner lenticular segment; the uncus, the optic tract (in its posterior half); the lateral choroid plexus; the endyma of the posterior and lower parts of the lateral ventricle; the greater part of the tail of the caudatum; exceptionally the external parts of the upper half of the thalamus.

But the posterior arm of the internal capsule is also in part supplied by the medicerebral and postcommunicant (the anterior third of this part by the latter vessel), the deeper parts by the prechoroid and postcommunicant, and the upper parts (above apex of midlenticular segment) by the Sylvian (lenticulo-optic ramus of Duret).

Circulatory disturbances in the supply territory of the prechoroid cause opposite hemiplegia by softening in the posterior segment of the internal capsule, involving the pyramidal and cranial-motor tracts.

Hemianesthesia, hemianopsia, and hemianosmia may likewise follow closure of the prechoroid, but are usually headed off by collateral supply.

When the postcommunicant is large, its blocking may cause opposite facial and hypoglossal paralysis, since these tracts traverse the front part of the posterior arm of the capsule.

The Medicerebral (Sylvian artery, *vide* Plate XIX. and Fig. 1003, 2).—The vessel represents the most direct continuation of the cerebral carotid. It lies at the bottom of the Sylvian fissure as do also the primitive portions of its larger branches as they spread out over the insula. When the postcommunicant starts from the medicerebral, the previous short (four to six millimeters long) portion of the latter participates in the circle of Willis. No branches are assigned to this part.

The medicerebral in its further course yields two classes of branches: (*a*) direct, perforating, or nutrient arterioles; (*b*) large and small pia arteries.

(*a*) A few perforantes (Fig. 1003, 5, 5) from the earlier part of this artery may pass directly to the caudate head with those described under precerebral and mentioned under carotid. But the main group from this source take a somewhat different course, and, as stated by Heubner, are often detached from the trunk farther out in the fissure. These have been divided into two sets. The first to leave the trunk—*lenticular arteries*—are the finer, and are similar in deportment to the preceding, except that they go to the first and second segments (apex) of the lenticular nucleus. The second, coarser set runs along the base of the lenticular nucleus on the limit of the external capsule. A portion of these pass caudad and dorsad to the thalamic extremity of the lenticular nucleus, and terminate in the thalamus—*lenticulothalamic arteries*. One arteriole, noticeably larger than any of the others and the frequent source of hemorrhage in this region, passes dorsad and mesad to the third segment of the lenticular, where it gives off many side twigs, and finally divides into four or five terminal branches, supplying also the adjacent internal capsule, etc. Two or three accompanying arterioles extend toward the third segment, and may attain the tail of the caudate. Collectively these are termed *lenticulostriate arteries*.

A further group might be made of the small direct vessels traversing the insula to gain and supply the claustrum; as this is, however, a derivative of the external gray layer, these twigs more nearly correspond to the general cortical and albal arterioles.

Of the perforants as a whole, it may be said that they all emanate at right angles from the inner side of

the mother vessel. Their size varies from 0.5 to 1.5 millimeters. They immediately enter the brain substance, only occasionally dividing, and never anastomosing before doing so. They usually run a further short course before branching. The ultimate distribution of each is pencil-shaped. They are destined to supply the central gray nuclei and the capsules, notably the inner. They are all true terminal arteries, without any anastomoses either between themselves or with other arteries. According to the French school, even their finest capillaries do not connect, but on this point the Germans teach otherwise.

(*b*) Pia branches of the medicerebral. After a course of 1 to 2.5 centimeters the main trunk, either at one stroke or successively, divides into several large branches.

1. Previously, however, there are usually a few small rami for the adjacent borders of the frontal, and especially the temporal, lobes (see Plate XIX.).

2. *Frontal* branch. This is generally the first large ramus. Like the succeeding, it runs some distance deep in the sulcus and subdivides, often at least, before appearing externally. It is especially destined for the subfrontal convolution. It supplies the orbital surface of the frontal lobe external to the orbital fissure, and the convexity dorsad to the middle of the medifrontal gyrus, caudad to the precentral sulcus. Duret found a very constant corresponding artery in several species of animals.

3. *Preparietal.* This nourishes the precentral and the adjacent extremity of the medifrontal convolutions, and may by an early branch include the postcentral also.

4. *Mediparietal.* This may gain the fissure of Rolando to supply not only the postcentral convolution, but dorsad a portion also of the precentral. It may also reach the adjacent parietal region.

5. *Postparietal.* This is a large branch in the horizontal Sylvian fissure. Its ramifications do not extend beyond the parietal or occipital fissure, but may pass beyond the supertemporal.

6. *Temporal.* This is included under the last by many, but it is often an early and large branch of the medicerebral. By its numerous considerable subdivisions it then covers practically the whole external temporal surface. At least the supertemporal convolution and much of the meditemporal are regularly supplied. Its distribution extends nearly to the suboccipital convolution.

There is no special artery for the insula, but it receives several small branches from the preceding as they cross it.

The Postcommunicant.—Connecting the pre- and post- (carotid and vertebral) systems. Each starts from the carotid or medicerebral, and runs directly caudad to inosculate with the corresponding postcerebral at five to twelve millimeters from the latter's origin. They pass ventrad of the optic tracts and also encounter the crura cerebri. In size and occurrence these vessels are variable, and frequently unsymmetrical. The left is more often the smaller or even absent, though some filiform anastomosis from a corresponding branch of the carotid usually does exist. As a very large branch from the carotid, especially the right, it may replace the corresponding postcerebral wholly or in part, or conversely; a large left communicant has been observed to arise from the postcerebral and supply the same medicerebral. Aside from disparity in size (forty-three times) the postcommunicants were normal in 175 of Windle's cases. Excepting slight anastomosis, both were absent in 3 cases, the right in 9, the left in 13. In 7 both were very small; in 28 the right was much larger than the left; in 15 the reverse.

Anomalies, says Bullen, are more common in the postcommunicants than in all the others. Of these vessels, either (1) may be absent; (2) may be replaced by a branch from the subcerebellar, internal carotid, postcerebral, or two small nutrient branches respectively from the last two vessels; (3) may supply unusual regions; or (4) may be unconnected with the carotid system.

This vessel gives off laterally pia branches, (*a*) internal, (*b*) external, and (*c*) inconstant penetrating rami.

(*a*) 1. Chiasmic branches to the caudal side of the chiasm. 2. Twigs to the tuber cinereum and infundibulum, a descending ramus supplying the pituitary body. 3. Two to the mammillary bodies.

(*b*) 1. To the optic tract. 2. To the cerebral crura. 3. Often considerable branches to adjacent temporal gyri.

(*c*) 1. *Prethalamic Artery* (internal and anterior optic of Duret). It penetrates between the tuber cinereum and mammillary bodies, and ramifies in the more anterior part of the aula, on the walls of the infundibulum, etc. 2. Medithalamic artery (posterior internal optic). At times large, it enters the postperforated space and passes directly dorsad near the inner thalamic wall, to which and the gray commissure it is distributed. This vessel comes as often from the postcerebral as from the postcommunicant. The prethalamic may also have the same origin.

The Postcerebrals, from the end of the basilar to the postcommunicants, complete the circle of Willis. This part furnishes: (1) three or four arterioles to the internal aspect of the crura cerebri, supplying its basal layer, the locus niger, etc.; (2) little branches entering the thalamus through the postperforated space. These accompany, and often include, the above-described medithalamic artery.

Windle found the postcerebral arteries normal in 173 cases. The vessel was derived from the carotid instead of the basilar in 11 cases on the right, 9 on the left, and 4 on both sides. There were 2 postcerebrals on the same side—the smaller from the basilar, the larger from the carotid—in 3 cases: 1 on the right and 2 on the left. Either of the postcerebrals may (Bullen) (1) be absent; (2) be a branch of the carotid system; (3) be replaced by a large postcommunicant; or (4) be replaced by two thread-like vessels from the basilar.

This trunk, in passing around the crus, describes a kind of semicircle, directed toward the transverse fissure. Dorsad of the crus, at about one centimeter from the optic lobes, it turns laterocaudad to gain the calcarine fissure, where it breaks up to supply the basilar postcerebral region. From its crural portions it supplies, besides other branches, nearly all the nutrient arteries of the celian walls.

1. Little twigs to the outer part of the crus, penetrating almost immediately. Instead of several in the thalamo-crural sulcus, there may be a single larger one, parallel to the main stem.

2. The fairly constant *Medioptic* (median quadrigeminal), giving fine offshoots in its course to the crus, and terminating in a bunch of fine vessels in the interval of the optic lobes.

3. *Postthalamic* (so-called posterior and external), two or three, or a single larger one, starting midway from this portion of the postcerebral, and following the crus to enter the thalamus between the geniculate bodies.

4. *Geniculate*, emanating directly, or from the thalamic.

5. *Postchoroid* (posterior and lateral), starting near the optic lobes, and entering between the layers of the velum. It always divides into two principal rami: a lateral one for the third of the choroid plexus not supplied by the prechoroid artery, *i.e.* for the plexus over the thalamus; the other more median one for the velum (*ramus velaris*).

6. *Medichoroid* (posterior and median choroidal), from the postcerebral at its nearest approach to the median line. It courses beside the conarium, to which it yields some rami, and immediately divides into two branches, one to the velum of the aula, the

other exclusively to the choroid plexus of the same cavity.

The choroid plexi and velum represent a double layer (fold) of the pia, within which the celian arteries and veins course. Duret states that in all the ventricles the arteries to the velum are distinct from those to the plexus, often even from their origin at the postcerebral, and always at their entrance into the corresponding cavity, and that they never mingle in their distribution. From the velar arteries are detached a multitude of little arterioles, which penetrate the thalamus 1 to 1.5 centimeters. They have the arrangement of cortical arterioles, and are pencillated. The two velar branches terminate in the head of the caudate, either simply subependymal or passing deeply into its substance. The velar branches to the aula emit little arterioles laterally at intervals of about a millimeter. These penetrate perpendicularly the adjacent wall. They supply also the posterior and gray commissures, and terminate in a fine pencil in the anterior commissure. The plexus arteries, on the contrary, do not usually participate in the nutrition of the celian walls. They divide into four or five long parallel branches from which little arterioles pass into the plexuses, properly speaking. They enter the little tufts by their base, and form very attenuated and sinuous capillary meshes. It has been suggested that they are the remains of former branches ramifying in the embryonic celian pia, and that they became coiled up when this membrane retracted.

7. *Preoptic* (anterior quadrigeminal), very short, coming from the most median part of the postcerebral, or from some branch of the latter. It forms a very delicate pencil over the preoptic body. This makes the third pretty constant pair of optic arteries, as these lobes are very vascular. They have some anastomoses across the median line.

8. Artery of the cornu Ammonis, oftener from some branch of the postcerebral than arising directly. It does not ramify on the celian surface, but passes between the Ammonshorn and the hippocampal convolution, to traverse the cortex in the manner of external arteries.

9. Variable branches to adjacent temporal gyri.

Final Divisions of Postcerebral.—These may be brought under three general heads (see Plate XIX.).

1. *Pretemporal* branches to the uncus in part, and the basal surface of the temporal lobe as far as the border of the convexity, except the third nearest the apex of the lobe, which is supplied from the medicerebral.

2. *Posttemporal* to the basal surface of the occipital lobe, including a variable amount of the adjacent temporal region, and doubling the border of the convexity to supply a little of the external occipital region. The hippocampus may be supplied from the parent stem, or from either 1 or 2.

3. *Occipital* artery. This runs along the calcarine fissure, sending a large branch through the occipital fissure; it supplies the cuneus and general median surface of the postcerebral lobe, and a considerable strip of the adjacent occipital convexity. Spitzka says that an artery large enough to cause fatal hemorrhage enters the gray and white of the right occipital lobe.

General Features of the Arterial Supply.—The distribution of each primary trunk includes: (*a*) basilar or nuclear branches; and (*b*) pial or cortical branches.

(*a*) These are the pre- and postperforating and celian arteries, arising in part from the circle of Willis. They supply the central ganglia, celian structures, and in part the centrum semiovale. To the same class belong the direct arterioles from the basilar to the nuclei in the pons. Excepting occasional and unimportant anastomoses, these are all true terminal vessels. They divide within the brain substance at an acute, and not a right, angle.

(*b*) The pial branches or divisions as described are only averages, complementary variations therefrom always being present; though it is claimed that while "their origin is often very variable, their distribution is constant." The larger arterial trunks correspond to the main fissures. To a marked extent it is true that the same branch does not supply both sides of a sulcus. Branches usually leave the parent stem at almost or quite a right angle. Some writers try to show a freer supply to the left hemisphere. Duret's attempted correlation of arterial distribution and physiological function was at least premature (1877) and faulty.

Ayer (1909) sums up his work as follows: "1. The Middle Cerebral Artery has *not* plainly the predominant share. It supplies, first, a limited part of caudate nucleus (back of the head); second, middle of lenticular nucleus; third, no part of optic thalamus; fourth, middle part of internal capsule; fifth, external capsule slightly.

"2. Anterior Cerebral Artery. Caliber of vessel equal to middle cerebral artery. It supplies constantly head of caudate. Supplies principally globus pallidus and anterior third of putamen; anterior third of internal capsule and external capsule slightly.

"3. Posterior Cerebral Artery not more important than anterior cerebral. It supplies optic thalamus largely.

"4. Choroid Artery from Internal Carotid Artery. It supplies posterior third of putamen slightly, globus pallidus and inner part of internal capsule.

"In forty-five examinations no case of lenticulo-optic artery was found, a result radically different from what has been accepted."

Antasomoses.—The basal circle of Willis comprises all the communications readily demonstrable on the uninjected pial arteries of the cerebrum. Only within this circle and over the optic lobes are there any minute connections across the median line of the hemispheres.

There has been a dispute as to the extent to which the ramifications of adjacent branches on either hemisphere are connected. Duret, after numerous, varied, and evidently careful examinations, says: "Never have we found an anastomotic network in the pia." He also notes the frequent superposition in the pia of fine arterial ramifications. Nevertheless he found considerable individual differences, and regularly some fine (0.2 to 0.25 millimeter communications, especially at the periphery, *i.e.* between adjacent territories of distribution. On p. 927 he acknowledges that in the great majority of cases, owing to anastomoses, "however rare and unimportant," softening from occlusion of any of the large basilar trunks spares the peripheral parts of the artery's territory. In the four-months fetus he found abundant fine anastomoses. Heubner (p. 174), on the contrary, says: "The chief (pia) branches end in a kind of communicating canal system or reservoir, which is spread out in the shape of a tubular net over the whole surface of the brain." By injecting "under weak finger pressure" he found plentiful anastomoses up to one millimeter in diameter. Heubner's description harmonizes with that of older writers, and is corroborated by Lucas, who by sufficiently penetrating injections was able to demonstrate an abundance of communicating arterioles up to 0.25 millimeter (*vide* Plate XVIII., Fig. 2). It remains true, however, that when the communicants of the circle of Willis are poorly developed, the peripheral anastomoses are, in a large number of cases, incapable of substituting them.

Direct or Nutrient Arterioles of the Convolutions.—These emanate at right angles from the pial branches, of all sizes. They penetrate the crests of the convolutions perpendicularly, the inclined surfaces obliquely. They are innumerable—scarcely more than one millimeter apart. According to size and distribution there are two classes:

1. Cortical, 0.05 to 0.03 millimeter in diameter. The finer stop in the cortex proper; the others go to the boundary of gray and white. The capillary network from these rami has been divided ito three somewhat differently characterized layers, each parallel to the rolling surface.

2. Albal (arteriolæ longæ), 0.08 to 0.14 millimeter in diameter. These are almost rectilinear, can be followed a distance of from three to four centimeters, and branch at an acute angle. They supply a considerable portion of the centrum semiovale. One often passes down along the axis of the convolution. A group of five or six at the bottom of a fissure (in section) diverge on entering. The capillary network of the albals is more elongated than that of the corticals, and accompanies the fasciculi of nerve fibers.

Both classes anastomose freely in their finer branches though in general pencillate.

From the anatomical arrangement it is believed that the intravascular pressure is less in the gray than in the white substance.

It has been claimed by many that the thyroid gland acts as a safety diverticulum to the cerebral supply.

Width of Brain Arteries.—To make a relative estimate of the capacity of the arteries at the base, Bevan Lewis ("Examination of Brain," 1882, pp. 20–22) determined their average diameters in 45 cases (insane). That of the vertebral was, r. 3.147 millimeters, l. 3.42; of basilar, 3.82; of postcerebral, r. 2.658, l. 2.56; of carotid, r. 3.951, l. 4.02; of medicerebral, r. 3.133, l. 3.55; and of precerebral, r. 2.73, l. 2.66. The sectional areas are of course proportional to the square of these diameters. As a rule, the united areas of branches equal very nearly the area of the parent trunk—excepting the preponderance of the vertebrals over the basilar (22.4 to 14.8).

Löwenfeld has found that the relation of the artery width to the brain weight is, even normally, somewhat variable, and that often, though not by any means in all cases, the width of the brain vessels rises and falls with the width of the aorta; moreover, that not rarely abnormally small brain arteries occur in otherwise well-developed arterial systems. He also made out a difference in the two sides, the left carotid being usually wider than the right.

Pressure in the Brain Arteries.—A further matter, noted by St. John Bullen (*loc. cit.*), may partially indicate the relative pressures in the main brain arteries. He remarked atheroma of the basal vessels in 410 of 1,565 autopsies, or 26 per cent. of the total. It was present to a considerable extent, either generally dispersed or in special trunks only, in 175 cases, and to a less extent in 235. The relative frequency by location was: medicerebral, 38 per cent.; basilar, 30 per cent.; postcerebral, 21 per cent.; carotid, 10 per cent.

Mendel (1891) has found experimentally that the pressure in the cortical arteries is materially less than that in the carotids, while that in the striatal arteries is not materially less. This he attributes to the fact that the latter are terminal vessels, though it is doubtless quite as much due to their less circuitous supply. He further thus explains the frequency of hemorrhage in the striatal region.

Tedeschi's conclusions regarding the brain arteries refer in part to moot points, but really contain nothing new and are deceptive in statement.

Veins.

The venous passages of the brain and its membranes include:

I. The dural veins.

II. The intrinsic veins, or those of the brain proper.

III. The sinuses.

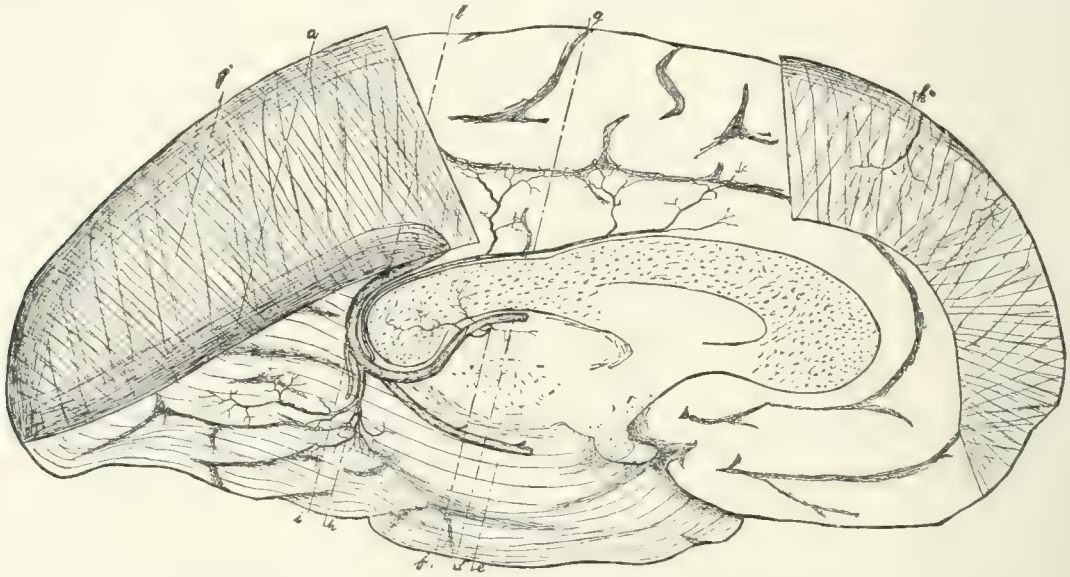

Fig. 1004.—The Vena Galeni. (From author's "Veins of the Brain," etc.)

IV. The venous exits from the skull.

All the intrinsic and most of the dural veins discharge into the sinuses, or appendatory spaces, which in turn convey the blood to the exits. Otherwise these two sets of veins are separate systems, not interanastomosing, unless occasionally near their mouths. The intrinsic veins without exception have thin, readily collapsing walls, while the sinuses are held open by the firm enclosing dura. In general it may be stated that *the walls of all these vessels are devoid of muscular elements*, though occasional unstriped fibers have been observed in the intrinsic veins. From this absence of actively contracting fibers, it follows that these vessels play a merely passive rôle in the encephalic circulation. The encranial veins, like the external veins of the head, are devoid of true valves. However, at the orifices of the diploë veins (Dupuytren, Langer, doubted by Trolard) and in the ophthalmodural vein, valves *may* occur. It has also been claimed that the supercerebral veins in part present a valvular arrangement at their discharge into the longitudinal sinus.

EXPLANATION OF
PLATE XVIII.

EXPLANATION OF PLATE XVIII.

FIG. 1.—Sinus Cavernosi et Intercavernosi—Sinus Circularis of Ridley.

Inferior aspect of a corrosion preparation from a child, with afferents and efferents (somewhat enlarged, and also arbitrary as to execution of smaller vessels). From Langer's "Der Sinus cavernosus der harten Hirnhaut," *Sitzbr. d. k. Akad.*, 1885, Vienna (Fig. 5).

V.o., Vena ophthalmica superior et inferior.

S.i.c., Sinus intercavernosi.

E, Emissary veins passing through the oval foramen to the pterygoid plexus.

S.p.i., Sinus petrosus inferior.

L, Space for the dorsum ephippii.

FIG. 2.—Fine anastomotic network between three arterial twigs in the pia of the parietal region. (Lucas, Paris Thesis, 1879.)

Fig. 3.—Lobule of a choroidal villus; one portion bare of epithelium. Sinuous vascular loop. Enlargement, 500 diameters. (From Luschka.)

a, Portion covered by epithelium.

b, Fibrillary connective tissue.

c, Structureless connecting substance extending well beyond the capillaries.

FIG. 4.—Very perfectly injected vessels of a choroidal villus. Two hilus vessels, a vein, and an artery. Loops, vascular nets, etc. Enlargement, 50 diameters. (From Luschka's "Die Adergeflechte des menschlichen Gehirns," 1855, Taf. ii., Fig. 2.)

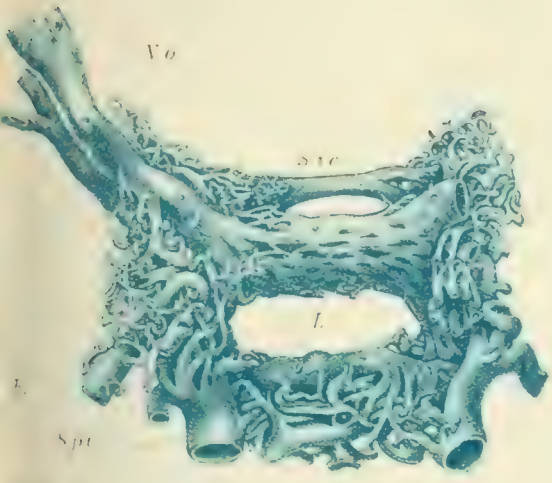

Fig 1

Fig 2

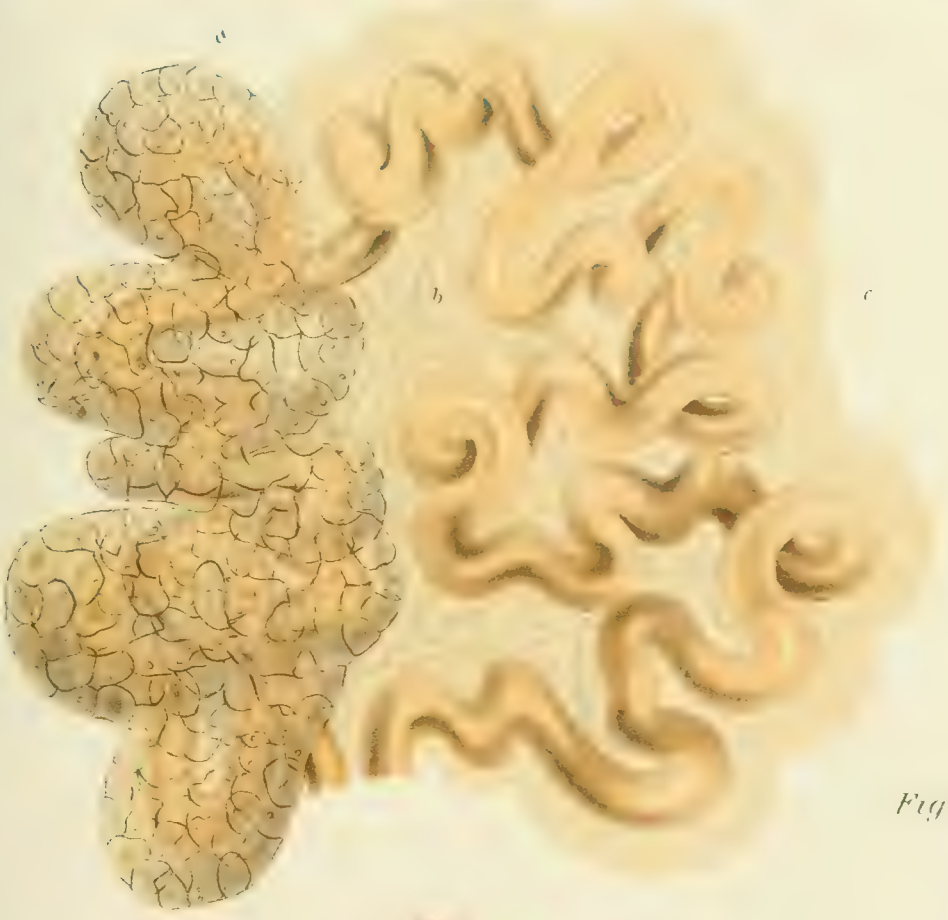

Fig 3.

Fig 4.

Brain-Vessels. (Vide Explanation at End of Article).

I. Veins of the Dura (including those of the diploë).—These are many in number, but all of small size. They anastomose so freely that they might almost be denominated a plexus. In position they are comparable to the plexus venosus existing between dura and periosteum of the spinal canal. In their ultimate distribution they form two vascular nets, according to Langer, one in the outer, the other in the inner, layer of the dura. The beautiful, almost regular, interlacing of the former, figured by Langer from the fetus, the writer is able to corroborate. By means of small veinlets penetrating the inner plate of the skull, the dural veins communicate extensively with those of the diploë. They include:

1. *Medidural,* or *Venæ Comites,* accompanying the medidural artery and its branches. The two on either side of an artery repeatedly connect with each other and with neighboring veinlets. The largest pair is about the common trunk of the artery. One of these passes externally through a basal foramen to the pterygoid veins. The other ends in the medicerebral vein or its temporal sinus, or directly in the sphenoidal or cavernous sinus, with which latter it usually at least connects. The diploic canals have some special openings into the larger medidural veins.

2. *Superdurals.* These appear in part as direct continuations of the preceding, and then are double. They pass to the longitudinal sinus, largely through the intermediation of its lateral spaces. Labbé suggests that the supra- and medidural veins may constitute a small collateral path between the long sinus and basal conduits.

3. *Falcial Trunklets* (Fig. 1004, *k*), running to the longitudinal sinus and to the falcial sinus when present, otherwise to the tentorial. The tentorials go to the lateral and tentorial sinuses, also in part by way of the parasinual spaces.

4. The numerous veinlets for the other dural arteries, *e.g.* in the occipital fossa, have a more independent course and end in adjacent sinuses.

Venous Canals of the Diploë, even less yielding than the sinuses. Breschet's description is somewhat modified by Trolard. The diploë is made up of little areolæ. These canalize in any direction, though in general ventrad to discharge near the base. These canals are quite unsymmetrical, and do not increase in size in their course, excepting where there are casual enlargements; areolæ, conduits, and lacunæ are lined with a smooth membrane. Generally the diploë begins to appear about the tenth year, though small straight veins are evident earlier. Resorption of the cancelli goes on continuously, and after fusion of the sutures they may pass from one bone to another. In the aged we find a sort of wide-spaced venous plexus, no longer canals. There are several exterior outlets and numerous interior ones. Even the one through the supraorbital notch passes to the ophthalmic vein and so to the cavernous sinus. Casual mention will be made of most of the special terminations.

II. Veins of the Pia and Brain Substance.—From their derivation and discharge, these vessels naturally fall into three classes: A. The supercerebrals, passing to the longitudinal sinus. B. The internal or Galen's system, tributary to the tentorial sinus. C. Basal veins, ending in the various sinuses of the base.

A. The *Supercerebral* veins return the blood from the convexity as far as the Sylvian fissure, and from the median surface of the hemispheres as far as the supercallosal fissure. There may be a slight interval between the frontal set and the others, or a smaller vein may here occur; otherwise they are all fairly equidistant. There are usually six to eight large trunks on each side. These veins tend to empty into the sinus in pairs. This is less marked in the frontal set. It is most easily demonstrable in the fetus, owing to the absence of Pacchionian bodies, or thickening, adhesions, etc., at the border of the convexity. The last pair ends in the sinus some three to five centimeters before the torcular. The second or third pair from the last may be somewhat larger than the others, and then represent the so-called anastomotic vein, though its size is quite as much due to the greater width of the brain in this part. Although Labbé says this vein runs along the postcentral fissure, it is probably identical with Krause's fetal *vena sulci centralis.* Moreover, each supercerebral vein is double, also best seen in the fetus. The two constituent veins are of unequal size, the larger external one coming from the convexity, the smaller inner one coming from the median surface (of hemisphere). They may soon unite to one trunk, but generally, in their further course to the sinus, they lie side by side within a common sheath, and do not lose their integrity as independent conduits until about to open into the sinus. Commonly some of the paired, as well as their constituent double veins, are wanting to complete the diagram.

The frontal set take a course very nearly at right angles to the sinus, or the first of them may even run caudad along the sinus before discharging. They usually spring over to the dura a couple of centimeters away from the sinus. This point has since been more carefully gone over by Mittenzweig. In 200 cases he found 59 in which the presupracerebrals (to only 9 in which the postsupracerebrals) jumped over from the piarachnoid to the dura at three or four centimeters from the long sinus—thus favoring their rupture, as he thinks. Farther along the sinus the veins take a more and more oblique course until they at last run forward a distance of three or four centimeters to discharge against the current. At the border of the convexity, or farther out in the pia, the vein makes the necessary bend to approach the sinus as described. It then runs a short distance in the pia, becomes in the fetus a free trunk for a further short length, and finishes its course in the dura.

Again, the frontal set open at the lateral angle of the sinus, while the others open more and more at the side, and the last quite at the bottom of the sinus, even coming up a distance through the falx.

Toward their field of derivation these trunks pursue an indifferently parallel course. In general, over the cortical area the finest veinlets are richly distributed everywhere, from the bottom of the fissures to the crest of the convolutions.

B. *The Internal System, Tributary to the Tentorial Sinus.*—Along its course this mesal sinus receives only unimportant, mostly dural, veinlets. At its commencement there may be two affluents: (*a*) the falcial sinus: (*b*) the vena Galeni.

(*a*) The inconstant *falcial sinus* also receives only dural twigs in its course, but at its commencement—opposite the frontal border of the middle third of the callosum—*may* take up a small vein or veins coming from the frontal third of the callosum, and from the bordering convolutions. Labbé calls this the *interhemispheric vein,* and says that the one to two centimeters long veinule bifurcates, sending one branch to either side. A parallel term, *mesolobica,* was given by Breschet to the precerebral vein.

(*b*) *Vena Galeni.* This discharges through a slit in the basal wall of the sinus, just caudad of the free border of the tentorium. The name is now limited to the short (one centimeter long, six millimeters broad) trunk from the union of the velar veins to the sinus. Within, it is often divided by a longitudinal septum.

The course of Galen's vein and that of the adjacent portion of the velars is very peculiar. The vessels sink a little after crossing the optic lobes, then encircle the splenium, and become subtentorial before ending in the sinus. The latter bears the relation thereto of a tangent to a circle (*vide* Fig. 1004).

Galen's vein does not usually receive any lateral affluents. It arises from the union of the right and left *velar veins*. Each of these consists of two portions, a terminal bent part (*portio curvata*, Fig. 1005, *c c*) from the conarium to the vena Galeni, and a peripheral, or celian, straight part (*portio recta*) from the origin of these veins, opposite the foramen of Monro. The two curved portions start and end together, but midway diverge 0.5 centimeter; they receive laterally many large branches. The straight portions run parallel and adjacent in the velum, but receive only few and small additions.

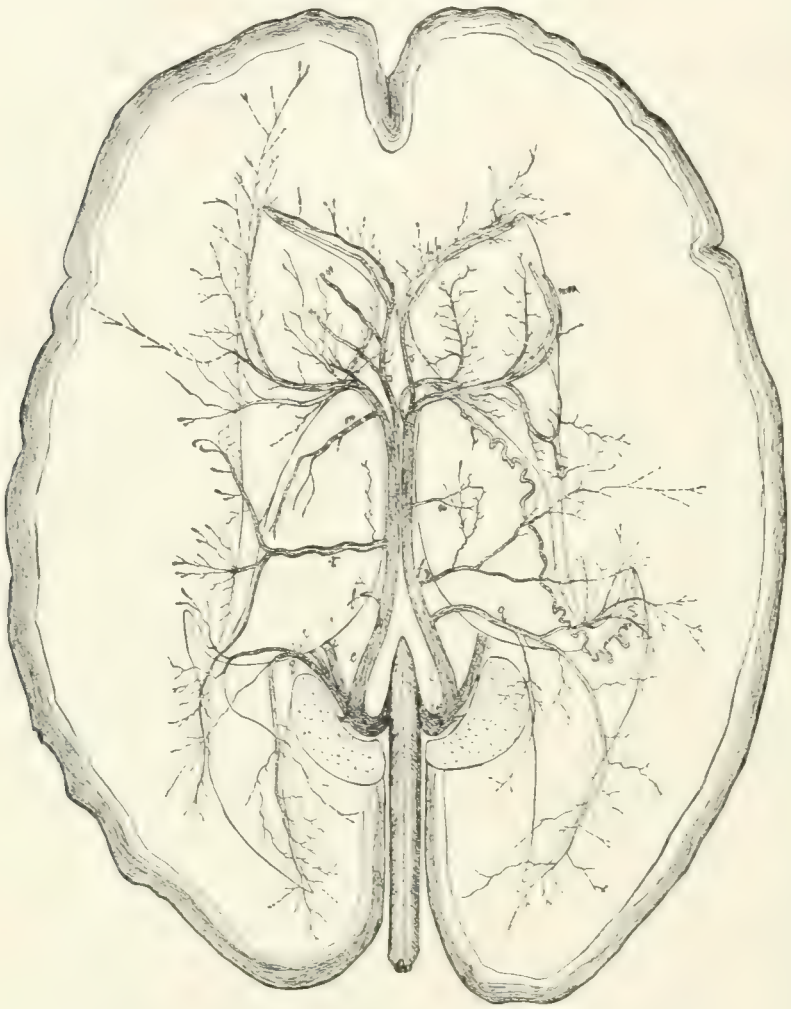

Fig. 1005.—The Celian Veins. (From the author's "Veins of the Brain," etc.)

The affluents to the portio curvata are largely of cortical origin; (1) v. suboccipitalis; (2) v. supercerebellaris; (3) v. callosalis; (4) v. subcerebralis; (5) vv. optici et conarialis; (6) v. postcornualis.

1. The *Suboccipital* vein (Fig. 1004, *b*) comes from the collateral fissure and median portion of the suboccipital surface of the cerebrum.

2. The *Supercerebellar* vein (Fig. 1004, *h*), oftener a single trunk, but occasionally bilateral, empties into the main vein near its termination, or even directly into the sinus tentorialis. It starts from many little branches over the dorsal surface of the cerebellum, the supervermis, and in its further course takes up small veins from the crura cerebri, and at times also from the optic lobes.

3. The *Callosal* vein (Figs. 1004 and 1005, *g*) (first mentioned by Labbé, 1879, then independently described by the writer in 1884) may be either single or bilateral. It is a small but long vessel, and the only one emptying on the concave side of the portio curvata. Its origin is near the middle of the callosum, and dorsad as far as the callosal fissure. It runs caudad at the bottom of the longitudinal fissure, and curves around the splenium close to Galen's vein. In animals (sheep) its size almost equals that of Galen's vein.

4. The *Subcerebral* (Fig. 1004, *e*) is a large vein, though its derivative territory is very variable. It forms by the union of many branches—collectively termed *Prebasal Veins*—opposite the preperforated space. The prebasilars include the first five next following:

(1) The *Precerebral* vein takes nearly the same path, but is too small and uncertain to be well compared to the precerebral artery. Its derivative area is very much less. It comes around the genu to the base, where it passes before the chiasm to the subcerebral vein. The right and left are usually of unequal size, but communicate though by an insignificant branch compared to the arterial precommunicant. The two veins may also unite before the chiasm and pass to one of the subcerebrals, in which case there are one or more slight connections in front of the chiasm with the other subcerebral veins. This vein receives branches from the genu and adjacent median frontal surface.

(2) The *Olfactory* is a tiny veinule, very constant, and demonstrable as far as the olfactory bulb.

(3) *Subfrontals.* One of these is frequently more developed, and may empty instead directly into the Sylvian or the medicerebral vein.

(4) The *Sylvian* vein, as shown by the writer, is distinct from and a variable complement of the medicerebral vein (*vide infra*). *It lies at the bottom of the basi-Sylvian fissure,* covered up, except near its termination, by the tip of the temporal lobe. It arises in the region of the insula from a great number of radicles. When the medicerebral is poorly represented, the Sylvian may take up twigs from the surface of the temporal and frontal lobes, some of the venæ perforantes pass, as a rule, to this vein. There is here often a group of perforantes, separated from the others and coming from the brain substance caudad of the veins.

(5) The *Venæ Preperforantes* are small, very variable in number, and take a straight course for a short distance before splitting up. They come from the striate nucleus amd adjacent frontal albalis. Their radicles approximate those of the precornual veins, yet without observable anastomoses.

(6) The subcerebral vein receives, in its course obliquely across the optic tracts and crura cerebri, several small veinules from the chiasm, infundibulum, mammillary bodies, crura, etc. These anastomose

freely with one another, and with those of the other side, thus making an outstretched network over these parts which connect on the one hand with a small network before the chiasm, and on the other with that across the pons. This corresponds in general to what Labbé terms the inferior interhemispheric veins. Frequently there are accessory veinules from the basal temporal surface.

(7) The *Subcornual* vein, in that it comes from the end of the middle horn, is comparable to the prechoroid artery. It is very constant in occurrence, but not in size. Though connected with the choroid plexus of the medicornu, it originates in the cerebral substance, sometimes even from the lateral wall of the postcornu, oftener opposite the caudal border of the thalamus, where branches are received from the albalis lateral to the thalamus or from other directions. In its course along the lateral wall of the horn it receives many accessions, notably from the cornu Ammonis, and as it curves around the end of the horn several twigs from the albalis of the temporal apex.

(8) *Postperforant*, at least one considerable veinule. The postperforating veins come, according to Hédon, from the cinerea of the walls of the diacele, and even from the mesal surface of the thalamus. He also claims that in the striate nuclei the perforating veins anastomose with those going toward the cavities and Galen's system. He further recognizes the communications in the medicornu between the choroidal and the infracornual veins.

(9) *Crural* branches, one in particular, can be followed along the crus to the cerebellum.

5. The fine *Conarial* vein and variable *Optic* twigs often end in the supercerebellar vein instead of directly in the velar. They originate in a fine venous plexus over the optic lobes and conarium, which appears to be connected across the crura cerebri with the basal network described above.

6. The *Postcornual* vein is variable, complementary in derivation to the subcornual. It may arise in the albalis near the tip of the occipital lobe, and then runs subependymal along the cornual wall. The parathalamic branches above ascribed to the subcornual, and some from the Ammon's horn, pass often in part to the postcornual. The radiate radicles of this vein are traceable through the albalis nearly to the cortex (Fig. 1005, *q*, *q*).

There is frequently another vein intermediary between (7) and 6, emptying into either the subcerebral or the postcornual.

The straight portion of the velar vein in its course through the velum receives the following, all at right angles:

1. The *Splenial* veins (Fig. 1004, *f*) are very small, and but two or three in number as they come out through the fornix. They often combine with thalamic radicles and empty as one trunk into the velar.

2. The *Thalamocrural* vein, usually one on each side, but sometimes multiple (Fig. 1005, *m*, *m*). This begins about the cerebral crus, makes its way dorsad and mesad through the thalamus, and joins the portio recta at about its middle point. It approaches the ventral side of the velar, and hence is but too easily overseen. Neither 1 nor 2 runs any length in the velum.

3. The *Thalamic* venules are very variable in size, number, and position. They may even be entirely wanting, or run to neighboring veins, *e.g.* the postcornual. These arise only to a limited extent in the thalamus; they come chiefly from the albalis beyond, running across or a trifle embedded in it. Where one of these is specially large it might be termed the *Transthalamic*.

Opposite or toward the apex of the thalamus, the velar vein is formed by the immediate or mediate union of several small trunks. Most of these are in a cluster coming in laterally between thalamus and striatum; the latter nucleus appears much richer in veins than the former. Of all but the first, the intracelial course of these veins is subependymal.

1. The *Medicornual* vein (Fig. 1005, *l*) takes a sinuous course in the outer edge of the choroid plexus, of about double the actual distance. Its membranous envelopment makes it a counterpart of the pial veins, and hence the actual continuation of the velar, as held by Bell. It begins in the middle horn, where it is said to anastomose with the subcornual. It comes out of the horn with the plexus, bends to follow the lateral thalamic border, and ends in any one of the veins near the commencement of the velar. Meanwhile it receives a multitude of radicles from the plexus, and some that seem to come from the surface of the thalamus.

2. The *Tenial* vein comes from the thalamostriatal groove, beneath the tenia. Nevertheless it has few tributaries from the thalamus. This short trunk is made up by three sets of venules: (*a*) *Striatal*. Of these there are usually two or three larger and several smaller branches, coming from the substance and surface of the caudate, and passing to the tenial trunk or to either of the following: (*b*) A prealbal trend of venules, passing along the outer celian border toward the precornu, and thence largely to the albalis of the frontal lobe. (*c*) An opposite trend, directly caudad, a short distance along the outer celian wall, and coming from the lenticular nucleus, the internal and external capsules, and the superimposed portion of the centrum semiovale. Many of these various albal radicles can be followed almost to the cortex; their angles of union are acute.

3. The *Paraseptal* trunk (Fig. 1005, *o*, *o*). This short vessel, with its two constituent *Precornual* veins, is the most direct continuation of the velar. Laterally it receives small *Septal* and *Genual* accessions. There are usually two parallel precornuals (*p*, *p*). They come from the extremity of the horn and follow its contour around to the septum, or run in the adjacent border of the caudate, though they take up no important radicles from that nucleus. Their multitude of radicles come from the albalis in the basal portion of the frontal lobe, also demonstrable nearly to the cortex.

4. The *Superalbals* (Fig. 1005, *n*, *n*) are commonly two small trunks that appear at the outer border of the ventricle, opposite the body of the caudate, cross the latter, and empty through the tenial or paraseptal trunk. They come from the celian roof, and the frontal and parietal albalis dorsad of those previously described.

C. *Basal Veins* (Fig. 1006).—These do not constitute a system in the sense of having a common point of discharge—in fact, they have already been described in part under Subcerebral Vein. Although they are quite irregular in termination—small veins seem occasionally to end at any point in the basal sinuses—still there are four frequent points of discharge: (1) Cavernous (and sphenoidal) sinus; (2) superpetrosal sinus; (3) middle of lateral sinus; (4) some sinus about the foramen magnum.

1. Some small veins from the pituitary body and other structures about the sella turcica have been described as tributary to the venous circle of Ridley. But the largest vein discharging at this point is the *Medicerebral*, a superficial vessel following the Sylvian fissure. This should be distinguished from the smaller though complementary Sylvian vein coursing at the bottom of the fissure. The medicerebral is inclined to be double, *i.e.* there are then two parallel adjacent veins, one taking up frontal branches, the other only temporal. In this case one vein may receive some of the prebasals above described and empty into the sphenoidal or the cavernous sinus, while the other runs mesocaudad in the dura across the temporal fossa to the middle of the superpetrosal sinus. This latter is the course that the whole medicerebral vein takes in many cases, as Trolard rightly

says; the dural portion may be termed the *Temporal Sinus;* by one or two lateral orifices it communicates with the medidural veins which it crosses.

2. The discharge of the subcerebral vein through the vein of Galen, as given above, holds for about one-half the cases—not always alike on the two sides. The main trunk may be diminished by the termination of some of its usual prebasal constituents in the cavernous sinus or medicerebral vein. Whether larger or smaller, the trunk as often passes to a basal sinus (superpetrosal) by turning ventrad instead of dorsad on reaching the cerebral crus.

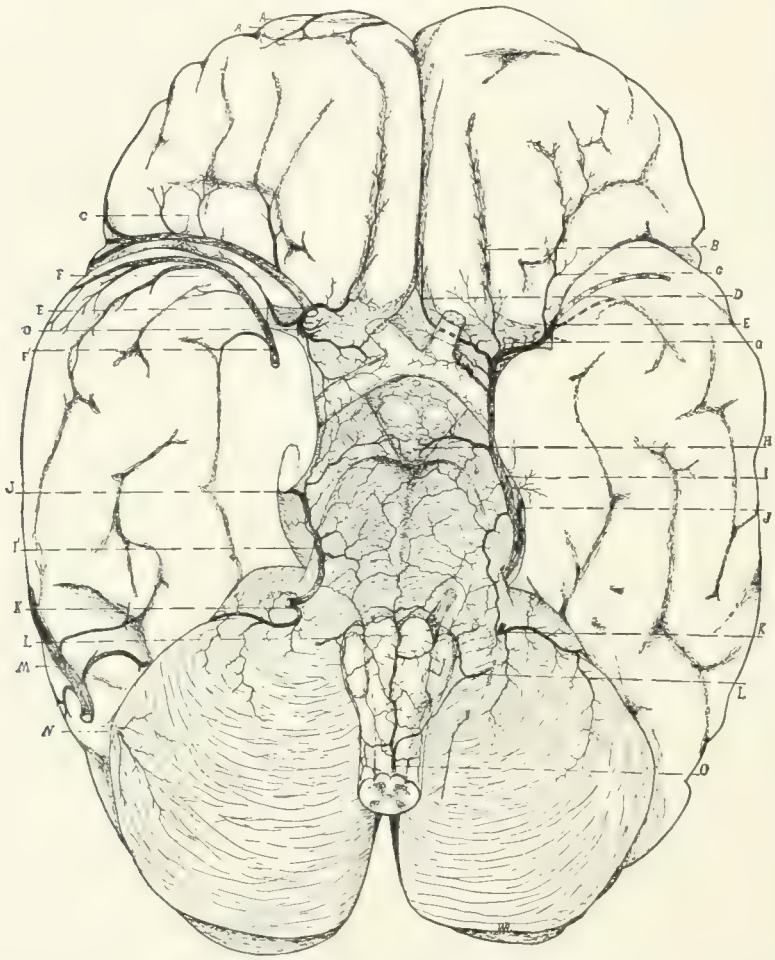

Fig. 1006.—Veins of the Base (three-fourths natural size). The two sides represent respectively the more common arrangements of these veins. Those of the myel and oblongata are largely after Kadyi. *A*, *A*, Supracerebrals; *B*, ramus to olfactory bulb; *C*, *C*, subfrontals; *D*, precerebral; *E*, *E*, Sylvian or insular; *F*, medicerebral (to cavernous sinus); *F'*, postmedicerebral (per temporal sinus to superpetrosal); *G*, *G*, preperforantes; *H*, postperforantes; *I*, subcerebral (to Galen's vein); *I'*, subcerebral (when emptying at base); *J*, *J*, subcornuals; *K*, *K*, precerebellars and flocculars; *L*, *L*, hypoglossals (to precondyloid emissary); *M*, postcerebral (to lateral sinus); *N*, paracerebellar (to lateral sinus); *O*, ventromyelic (anterior spinal).

One or more *Precerebellar Veins* from the flocculus region (*Floccular Vein*) pass to the superpetrosal sinus, with the subcerebral vein, when this terminates at the base; otherwise they seem to connect with this by venules along the lateral surface of the cerebral crus. Among the cerebellar veins Hédon, referring to Merkel, mentions one that "comes from the flocculus and empties into the superpetrosal sinus. An important branch of this vein rises from the interior of the cerebellum in the region of the dentatum, receives also veins from the cerebellar medipeduncle, and emerges with the peduncle under the flocculus. The main trunk can acquire a very considerable size when it receives a branch of the basilar vein" (precerebellar vein, Fig. 1006).

3. The *Postcerebral Veins* (Fig. 1006, *M*) usually unite into one trunk at the point where, turning caudad, they form an ampulla in the dura and enter the sinus. This is at the lateral border of the occipital lobe, opposite the exoccipital fissure. These veins come in part from the convexity, in part from the basal surface of the occipital lobe. The latter may be single or multiple; their derivative area is lateral to that of the suboccipital vein. The former is represented by one large trunk from the direction of the Sylvian fissure; it receives varying temporal branches and larger ones from the external occipital surface. The *Paracerebellar Veins* are smaller than the postcerebrals, but often empty opposite them, though, of course, subtentorial in origin. They come from the lateral portion of the cerebellum. The very inconstant *Postcerebellar Veins,* one or more in number, terminate in the lateral sinus near the torcular, or even in the tentorial.

4. The *Subcerebellar Veins* include any small vessels at the bottom of the posterior fossa discharging into the occipital sinus.

The cerebellar veins—supra-, pre-, para-, post-, and sub-—are but partially distinct from the cerebral veins.

Oblongata Region.—The ventromesal chain of myelic veins (see Fig. 1006, *o*) is continued cephalad on the ventral surface of the oblongata to the furrow between this and the pons, there connecting with a fine venous network over the surface of the latter (Kadyi). This plexus in turn also connects with the veins of the cerebellum and of the base forward.

Besides irregular smaller ones, there are in particular two constant and considerable veins passing from this plexus, one on either side along the trigeminal nerve to the sinus petrosus (or cavernosus).

From the above-mentioned chain on the ventral surface of the oblongata, between the pyramids, there frequently arises a little trunk (up to 0.5 mm. or more thick) that joins one of the hypoglossal root bundles and passes out with it through the precondyloid foramen—doubtless a part of Luschka's plexus venosus hypoglossi.

The dorsomyelic chain of veins is continued cephalad over the oblongata. From a constant mesal vein here a small venule traverses the arachnoid, covering the cisterna magna. Sometimes this adjoins the accessory nerve, and Kadyi thinks it probably empties into the sinus plexus about the foramen magnum.

General Features of the Intrinsic Veins.—*Communications.*—In this regard the pia veins must be distinguished from those of the brain substance. In contrast to the arteries, the pial veins communicate freely, not only indirectly through the sinuses, but

everywhere on the surface by a network of small vessels, as well as frequently by anastomoses between larger trunks. The veins of the convexity might almost be said to radiate from the Sylvian fissure (horizontal Sylvian). At least several of the larger ones connect toward the middle of the convexity. Of these, four may be specified: (1) One of the frontal supercerebrals (frontodorsad); (2) the second or third from the last supercerebral (caudodorsad); (3) the external trunk of the postcerebral (caudoventrad); (4) the medicerebral (frontoventrad). Or any two of these trunks may communicate independently, *e.g.* the medi- and postcerebral veins by a large anastomosis directly across the temporal lobe (intrapial, of course). There are many other connecting veins, not as markedly bridging the fissures, however. The great anastomotic vein of Trolard is No. (4) (medicerebral) when continuous with No. (2). Labbé's illustration includes also No. (3). Trolard says it "sometimes takes origin at the side of the longitudinal sinus, but oftener it forms by the union of veins anastomosing at the middle part of the convexity." He encountered it twenty-five times in thirty subjects. According to Labbé this anastomosis, instead of being with the medicerebral, may, in its absence, be with the deeper Sylvian vein. Practically these various anastomoses present a collateral path in the pia, between longitudinal, lateral, and cavernous (sphenoidal or superpetrosal) sinuses. The basal veins, excepting the perforants and the cerebellars, have ample though smaller anastomoses, including an indifferent counterpart of the circle of Willis. It is evident that the derivative area of the pial veins can never be closely defined.

The internal system must be separated into those veins uniting in the curved portion of the velar, and those tributary to the straight portion. The former, as the writer has elsewhere shown, have the following sets of anastomoses: (1) Between the callosal vein—including practically the rare interhemispheric vein—and the median branches of the supercerebrals, across the callosal fissure; (2) between the suboccipital vein and the basal branches of the postcerebral; (3) between the supercerebellar and other cerebellar veins; (4) between the subcerebral vein—when, as in about one-half the cases, this discharges into the velar—and the many veins adjacent to its derivative area. These communications are all in the pia; from clinical cases we know that these may suffice to compensate fairly when *only* the tentorial sinus and the short common vein of Galen are closed. They do not suffice, however, when there is any impediment to this collateral discharge, and possibly not when the subcerebral vein ends elsewhere. Of the veins passing to the portio recta of the velar vein, only one, the medicornual, has superficial anastomoses. As this is a long, tortuous vessel, and connects with the subcornual only by small and questionable anastomoses, it is of itself entirely unable to compensate when the portio curvata becomes occluded. We have, remaining, the various celian veins coming directly from the brain substance, to which the postcornual may also be added. Neither between these nor between their subdivisions short of the ultimate capillaries did the writer succeed in finding any anastomoses. The same holds true for the perforating veins of the base. There still might be intrasubstantial connections between these vessels and the cortical venules. However, the apparently positive results of injections by Duret, and especially by Labbé, are all explicable by the surface anastomoses above described. There may be such occasional but inadequate connections paralleled by the rare ones between the otherwise terminal perforating and celian arterioles. Hédon (1888) says that a few do exist. Clinical evidence also goes to show that the veins emanating from the celial walls are all essentially terminal vessels, and that closure of the velar vein—unless just at its mouth—cannot be compensated.

Cortical Venules.—Duret found only six or eight in the section of a medium-sized convolution, one or two emanating perpendicularly at the dorsum of the gyrus, and from four to six by the sides. However, they had a diameter triple that of the arterioles, They start principally from the capillary transition plexus—between gray and white—and from the deeper albalis.

Developmental.—From various peculiarities in the vascular supply of the human brain, more especially the caudad displacement peripherally of the postsupracerebral veins, the writer has adduced evidence favorable in a general way to Hill's theory of a developmental rotation of the brain, and showing further that in any such rotation the brain and pia have glided caudad under the dura and brain case.

Here may be added a casual observation of a persistent fetal form, made at the autopsy of a child of twenty-two months, dead of tuberculous meningitis. The large left medicerebral vein took the temporal course in a deep groove (per temporal sinus, intradural), and passed out at the foramen jugulare spurium instead of passing to the suprapetrosal sinus, first, however, connecting with a much smaller prepetrosal sinus. No such appearance on the right.

General Relations of the Veins and Arteries.—In the pia, over the convexity and on the median surface, the arteries lie beneath the veins (Labbé), as generally in the body elsewhere. But over the insula, and evidently in the sulci generally, the writer has observed the reverse; while of the finer pial arborizations Labbé asserts that the venous lie beneath the arterial. Though the larger veins often jump across from one gyrus to the next, the arteries go down with the pia more or less deeply into the fissures, to come up near or distant over the next gyrus.

Only by a forced comparison can any of these veins be said to accompany the arteries. By contrast, the dural vessels conform in their general bearing to those elsewhere; they have abundant collateral anastomoses, most of the arterial branches are accompanied by two veins, etc.

Dwight quotes the suggestion that, as the blood in the internal jugular and carotid flows in opposite directions, the arterial pulsations might interfere with the venous discharge, if both lay in a common canal. Trolard drew a strong analogy between the vertebral artery, surrounded by the vertebral vein and plexus, and the carotid through the cavernous sinus. "The supply arteries of the encephalon bathe (?) in venous blood; the carotids from the moment they enter the carotid canal; the vertebrals from the moment they penetrate the vertebral canal." This point has been elaborated by Rüdinger (*vide* abstract in *Boston Medical and Surgical Journal*, 1888, ii., 323). He shows that by this cushioning the pulsatory movements of the arteries are not abolished as they would be if they filled the bony canals. The diameter of the carotid canal he gives as 5–7 millimeters; that of the artery, 3–4.3 millimeters. In the cavernous sinus the artery, though situated at one side of the cavity, is not in contact with either the bone or the dura.

The various retarding bends and angles in both classes of vessels can only be referred to. They affect very unequally the circulation in the different parts. The existence in the pia of vessels larger than capillaries, connecting the arteries with the veins, has been many times asserted and denied—the last investigator, Labbé, contriving to do both. This point still awaits final settlement.

III. The Dural Sinuses.—The encranial sinuses are all intradural, and all except the tentorial (with the falcial) lie against the cranial wall. They do not collapse on being slit open, nor do they admit of

much distention—the falcial and the parasinual spaces excepted. They are lined by a continuation of the inner membrane of the jugular. Allen counts 16 sinuses—10 paired (symmetrical), and 6 unpaired (azygous). But their number depends so much on the way they are divided as to cause the remark that the easiest piece of anatomical work is to describe a new sinus.

They have been variously classified: (*a*) In two reciprocally perpendicular planes, the vertical plane including the longitudinal and tentorial (plus falcial), the horizontal including the remaining; or (*b*) in three horizontal planes; or (*c*) as connecting at three points, viz., the torcular and the two cavernous sinuses (to which Trolard sought to add a precondyloid confluens); or (*d*) according to the area drained.

The Longitudinal Sinus.—This, the longest sinus, runs parallel to the sagittal suture, slightly grooving the bone in a curved line from near the crista galli to the internal occipital protuberance. It lies between the folds of the falx, as they diverge to continue as the parietal dura. Its section presents a rounded triangle, increasing in size from the accession of large veins. Its lumen toward the bottom is crossed by numerous irregular strands (trabeculæ, chordæ Willisii). The openings from the supercerebral veins are usually larger than those from the parasinual spaces (and dural veins). The sinus subalterni of Malacarne are often seen in the falx just beneath the sinus, and present more or less developed parallel narrow passages freely connecting with the main vessel. At the torcular this sinus more often turns into the right lateral. Rarely it, or its tributaries, drops down through the falx to the falcial sinus, or just before the torcular to the tentorial, or even divides, following the lambda sutures to each lateral sinus. The whole longitudinal sinus may be occluded without causing disastrous results.

Falcial Sinus.—This may run along about two-thirds of the free border of the falx or near the border, and then represents the continuation of the tentorial sinus. It is rather a large dural vein than a sinus. At its commencement the occasional interhemispheric veins empty. Its only lateral tributaries are usually small dural venules, though part of the supercerebral veins or of the longitudinal sinus have in rare instances been seen to turn this way. On the contrary, Knott once saw the falcial pass to the longitudinal, and some connection between the two is not uncommon.

But, as stated by Luschka, this sinus is very variable in size and occurrence. In a series of adult subjects the writer found that its average occurrence was only one in six; in the fetus it was never present. Trolard's attempt at presenting this is an important anastomosis between the dorsal and internal systems, or as a safety diverticle of the latter, was quite overdrawn.

Tentorial Sinus.—This lies at the junction of the falx and tentorium (Figs. 1004 and 1005, *a*). It extends in full size from the torcular to the intersection of the free falcial and tentorial borders opposite the point where it receives its main tributary, the vein of Galen. Its section is a triangle with narrow base resting on the tentorium. Laterally it takes up small dural radicles, and often a supercerebellar vein. It is straight, lies in the median line, and is directed caudad. "It opens into the lateral sinus by an oval mouth formed by strong pillars of fibers."

Torcular.—A *confluens sinuum* in the sense of the old writers does not exist. "The right lateral sinus for the most part begins higher than the left, and may be considered as the continuation of the longitudinal. In some subjects the right or left lateral sinus begins from the longitudinal one, while that of the other side is continuous from the tentorial; and then the lateral sinuses are separated at their origin by a membranous isthmus" (Charles Bell, 1827). Rüdinger speaks of a "valvular arrangement" separating the two currents. In 26 out of Knott's 44 cases, the tentorial opened into the left lateral sinus, in 6 into the right, in 12 mesially. The statistics given below on the larger jugular canal bear on this question. This peculiarity of the paths at the torcular tends to prevent a reflux of blood from one into the other, or any interference of the currents.

However, in a considerable minority of cases the currents must intermingle. From the arrangements of the sinuses at the torcular, thrombosis of the longitudinal and right lateral is more often associated than of the longitudinal and left. A comparison of the few casual cases at hand shows 6 of the former to 2 (or possibly 3) of the latter. Of course, much more frequently—in 12—all three sinuses were involved.

Lateral Sinus.—This runs from the torcular, at first in the attached tentorial border, then curves (*flexura sigmoidea*) to follow the groove in the mastoid and gains the jugular canal. It has been seen to take a more basal course, running first in the cerebellar falx, then beside the foramen magnum to its usual exit. From the extensive investigations of Hartmann, Rüdinger, Bezold, and Politzer, it appears that frequently the sigmoid portion approaches within a few millimeters of the posterior wall of the auditory meatus. The one into which the longitudinal sinus turns, usually the right, is double the size of the other, and also a trifle longer. Rarely, one lateral is minimal in size or even absent. It receives laterally the postcerebral and paracerebellar veins and superpetrosal sinus, and gives off two inconstant emissaries.

Körner (1889) has shown that intracranial disease from caries of the petrous is more frequent on the right, and from a study of 449 skulls he attributes this to the fact that the lateral sinus at its sigmoid flexure enters deeper into the mastoid and the petrous pyramid on the right than on the left, and thus on the right approaches nearer the primary focus of disease. In 22 cases on the right and 8 on the left, there were gaps in the bony partition. He also holds that in the brachycephali the sigmoid excavation goes lower and deeper than in the dolichocephali, and that hence in the former such encranial sequelæ follow more readily; but this has been disputed by Schilzke.

Birmingham of Dublin (*Brit. Med. Journ.*, 1890, ii., 683), from an examination of 100 recent dry specimens, points out that the relations of the lateral sinus to the surface are extremely uncertain, owing both to variations in the sinus curves and to irregularities in the bones. It begins opposite the external occipital protuberance in 50 per cent.; lower (by never more than one-half inch) in 33 per cent.; and higher in 17 per cent. It does not run forward horizontally, but is distinctly arched. The bend of the sinus where it turns down at the asterion may vary, within wide limits, from a gentle to a very sharp curve. It then runs down in front of the postmastoid margin, about one-half inch behind the meatus, and turns into the rugular foramen about one-quarter inch below the level of the meatus floor. Occasionally the sinus is only one-twelfth of an inch from the surface.

Cavernous Sinus (Plate XVIII., Fig. 1), distinguished by its irregular outline and cellular or reticulated appearance from intercrossing fibrous bands. It represents a colossal perivascular structure about the carotid, in a way similar to that established by Braune and his school for certain lymphatics accompanying veins. The late von Langer, in one of his last publications, based on corrosion and other preparations from infantile subjects, showed that the cavernous sinus is originally a plexiform network of veins, which, by fusion of its channels, takes on its later characteristics. The wall resorption goes on to old age, when villous offshoots of the remaining trabeculæ are often seen to project into its cavity. It is traversed by the carotid (cavernous portion). All the orbital nerves except the optic pass near or through its outer wall. Besides veins and emissaries, it is the communicating center for all the prebasal sinuses. Frontad it tapers to the ophthal-

mic vein—the swollen end of which has been dubbed *Sinus Ophthalmicus*.

Laterally, the cavernous receives the *Sphenoidal Sinus*. This runs out along the dependent side of the lesser sphenoidal wing. Knott notes great variability in its size, though never complete absence, a small vein at least being found. Peripherally it receives or connects with a medidural vein, and also a diploic canal, and may take up the medicerebral and connect with ophthalmodural veins.

The *Subsphenoidal Sinus*, on the great wing of the bone, was found by Knott fourteen times on the right and nine on the left side.

Mesad, the cavernosi connect by the two *Transverse Sinuses*—which alone deserve to be called transverse. These follow the walls of the sella turcica, curve slightly to enclose the pituitary body, and complete the so-called circular sinus of Ridley (Plate XVIII., Fig. 1).

Sinus Præpetrosus (jugularis spurius of Luschka, petroso-squamosus of Hyrtl, petrosus anterior of Bell). This occasional sinus, at the bottom of the temporal fossa, describes a curve along the petro-squamous suture, from the spinous foramen—connecting with the medidural vein and also with the cavernous sinus—to either (or both) the emissarium temporale or the petrous portion of the lateral sinus (often by perforating the prominent petrous ridge). Its physiological interest arises from the prominent part which it plays in the fetus. Zuckerkandl (1873) found this sinus 22 times in 280 skulls. Knott, 4 times in 44, found what appears to have been a continuation of this sinus to the sphenoidal; in 7 of 44 subjects he found the prepetrosal on both sides, in 19 on one side only.

Caudad, the cavernous empties into the oblique super- and subpetrosal sinuses, but principally the former. The *Superpetrosal Sinus* starts from the cavernous, runs in the prolonged attached border of the tentorium along the dorsal ridge of the petrous bone, and enters the lateral sinus against the current at the beginning of its sigmoid flexure. It alone offers a direct encranial connection between the prebasal and lateral sinuses. The temporal sinus (medicerebral or anastomotic vein) and the subcerebral vein discharge into this in nearly one-half the cases, the precerebellar vein more constantly. As a consequence, its size varies considerably, though it is usually small. The vestibular and even tympanic veins of the ear pass to the superpetrosal sinus, either directly or by a dural vein. In his forty-four subjects, Knott notes its absence twice on the right and once on the left.

The shorter *Subpetrosal Sinus* runs in the petro-occipital groove, from the cavernous sinus to the subpetrosal vein, which, by bending before its discharge into the jugular vein, secures an unimpeded outlet for this sinus (for connections, *vide infra*, Vena Subpetrosa).

Occipitobasilar Plexus.—In the occipital fossa are several sinus canals that vary much in size and distribution. The *Occipital Sinus*, usually bilateral, runs along the cerebellar falx and connects with the lateral sinuses by small mouths beside the torcular. Pre-, trans-, and postoccipitals have been made out. The so-called circular sinus of the foramen magnum is more often incomplete dorsad of the hole. The basilar sinuses over the like-named process connect with the preceding and with the prebasal sinuses. Langer has shown that, like the cavernous sinus, all of these are the persistent channels of what originally, in the fetus, was a vein plexus; and he has also corroborated Virchow's description of their enlargement in the aged.

Parasinual Spaces.—These areolar venous pockets or derivative reservoirs (lacunæ, *recessus lateralis*), though described with increasing definiteness by a long series of observers, find but little mention in the text-books. Their principal development is opposite the middle of the longitudinal sinus (bilateral). As numerous minute spaces they further occur along nearly the whole length of the said sinus, and also (Langer) beneath it in the falx, beside the lateral sinuses, on both sides of the tentorial sinus, and it is said even about the cavernosi. The dilated intradural termination of the postcerebral and paracerebellar veins has also been thus classed. They all occupy the attenuated space between the dural layers lateral to the sinuses, and hence are very shallow and of irregular outline. They have a lining membrane, also many intercrossing fibrous filaments, and are injectable from or with the sinuses. In position and characteristics they are intermediary between dural veins and sinuses. Where present they receive most if not all the dural veins. The larger spaces are traversed by incoming pial veins with which they connect by one or more openings. They increase in size as life advances, and then have intimate relations with the Pacchionian granulations—so much so that they have even been termed Pacchionian blood cavities. The circulation in their interior is not believed to be very active and the spaces have repeatedly been found thrombosed.

On opening a sinus or the jugular canal blood usually flows out in a more or less pulsatory stream showing that the ruling interior pressure is positive. In the cases of operative perforation of a lateral sinus (usually ending in recovery) there is no record of air being aspirated. But in one case of opening of the longitudinal (Genzmer, 1877) so much air was aspirated as to prove quickly fatal, and Francois-Franck (1881) has endeavored by experiments to show that aspiration can be communicated through the vertebral veins to the diploic canals of the occiput.

Occlusion.—Blocking of any single sinus is not necessarily dangerous, though occlusion of a cavernous or the tentorial is always a serious matter.

By experimental blocking of the dural sinuses in the dog Ferrari (1888) has shown that a large part of the whole sinus system, *e.g.* all the sinuses of the calvarium, may be rendered impermeable without injury to the functions of the brain. However, occlusion of the collective blood efferents from the skull is of course quickly fatal, being usually preceded by an epileptic attack. But all this and more had been already determined by clinical experience in man.

IV. Venous Openings through the Skull (Emissaria, etc.).—From their number and pathological importance, and for clearness of description, these passages ought to constitute a separate class. Each of the cranial bones (except the ethmoid) has a foramen permitting direct communication between the dural sinuses and veins and the exterior veins; still these are of very unequal size, and in part disappear in the adult. There is but little topographical correspondence between the position of these exits and the area drained through them; nor is the area in any case closely definable. They may all act as efferent vessels, although the ophthalmic veins are usually afferent—partially so, says Sesemann, 1869; largely so, Gurwitsch, 1883, and Merkel—and certain of the others may conduct either way according to circumstances. Only Nos. 2, 6, 7, and 8 are superficial, while 7, 8, 11, and perhaps 4, belong rather to the dural and diploic system. Nearly all the blood normally passes out through the two postlacerated foramina with their four canals. But any one of the exits and, so far as known, any two—or in case of the smaller emissaria, several—may be permanently closed without causing serious harm. Both internal jugulars have been tied in the same subject (Pilger, 1880), without other evil consequence than a temporary headache.

1. *Jugular Canal.*—In the lateral part of the postlacerated foramen. This, by far the largest of all the

exits, leads from the sigmoid flexure of the lateral sinus to the bulb or gulf of the internal jugular vein. Its path through the foramen is often more or less separated from the passing nerves, etc., by a bony septum, thus forming a true jugular foramen. Rarely it is very small on one side, or even absent (four or five known cases).

By adding the series of 159 skulls examined by Dwight to the 100 by Rüdinger, we have 259. In 173 of these the right jugular foramen was larger than the left (*i.e.* about two-thirds), in 65 the reverse (one-quarter), and in 21 the two were equal (one-twelfth). This harmonizes with what was said above (*sub* Torcular).

2. *Emissarium Mastoideum*, of most importance in fetal life. It arises directly from the lateral sinus, and empties usually into the occipital vein (extracranial), sometimes into the postauricular, or even directly into the external jugular. In the 16 perfect skulls examined by Green (*American Journal of Otology*, 1881, vol. iii., p. 96), it was absent on both sides in 1, and on one side in 1. It was always just behind the posterior limit of the mastoid process. The external opening was opposite the meatus (at about the middle of the perpendicular height of the mastoid) in 20, above this in 2, below in 6, and directly on the base of the skull in 1. Its diameter measured 5 mm. in 1, 4 mm. in 4, 3 mm. in 10, 2 mm. in 10, and 0.5 mm. in 4.

3. *Emissarium Postcondyloideum* (postjugular vein), passing from the lateral sinus near its termination to the upper cervical or vertebral veins. In 44 skulls, Knott found this on both sides in only 13, on the right in 21, and on the left in 10. In Dwight's series of 142 skulls, with unequal jugular foramina, the postcondyloid foramen was larger on the same side as the larger jugular in 53, on the other side in 37, and equal or absent in 52 (this foramen being wholly for the transit of the emissary).

4. *Emissarium Precondyloideum*, connecting with the occipital sinus or its basal prolongation, taking up a diploic vein, and passing in part to the prepetrosal vein, in part to the plexus about the vertebral. As plexus venosus hypoglossi, Luschka described a cluster of veins about the hypoglossal bundles as they unite in the inner portion of the foramen, from which two veins passed down the canal. Trolard says that externally the precondyloid foramen presents a deep cavity in which is lodged a true venous confluens. Ventrad its wall is hidden by the external part of the atlo-occipital ligament. He says that this confluens receives five veins: (1) Ventrad and mesad, the medilacerate; (2) lateroventrad, a connection with the subpetrosal vein; (3) dorsad, a precondyloid vein; (4) laterodorsad, an inconstant vertebral vein (passing between atlas and occiput, behind the internal jugular, sometimes in a bony canal); (5) a little vein on the preatlo-occipital ligament, communicating across with the intraspinal sinuses.

Dwight, in the same series of 142 skulls, found the precondyloid foramen larger on the same side as the jugular in 16, on the other side in 11, the two sides equal in 115. "There does not appear to be any definite relation between their size and that of the postcondyloids."

5. Small uncertain veins through the *foramen magnum* or beside the vertebral arteries, connecting some marginal sinus or vein with the vertebral and spinal vessels. The fine veins in the spinal cord also connect with interstitial ones above.

6. *Emissarium Occipitale*, a small mesal conduit from the torcular through the occipital protuberance to the external veins of the occiput. It is often, but not always sinuous, and takes up an azygoid diploic trunk. Knott found it as a small but traceable vein in 6 of his 44 cases. In most of the others there was a small vein piercing one of the bone plates and anastomosing with the diploë veins.

7. *Emissarium Parietale.*—In 100 skulls Gruber found the parietal foramen on both sides in 29, on the right in 19, on the left in 12; average distance from angle of occipital squama, 3–5 centimeters; distance from sagittal suture, 2–17 millimeters. Their size varies ordinarily from ½ to 1 millimeter. They do not terminate internally directly in the long sinus, but in the parasinual spaces or dural veins.

8. *Diploic Connections.*—Innumerable small openings through the inner plate of the skull connect the dural veins and spaces with the diploë canals. These are largest and most numerous along the longitudinal sinus (author's corrosion preparation).

9. *Orbital Connections.*—(*a*) The ophthalmic vein is, next to the jugular, the largest and most constant of all the passages. It empties largely into the cavernous sinus (through the orbital fissure, where it bears a constant constriction), but has free anastomosis with the prefacial vein at the inner canthus. Allen says that formerly the trunk of the facial was opened at this point to relieve cerebral congestion. (*b*) The central retinal vein has full anastomoses with the ophthalmic, but goes as a rule to the cavernous sinus, or frequently to a fine venous plexus around the optic nerve, and then by several venules in part to the subophthalmic vein, in part to the said sinus. (*c*) The smaller subophthalmic vein or veins connect doubly with the larger into which, or oftener into the sinus cavernosus, they discharge (always afferent, say Sesemann and H. Meyer). Peripherally, they anastomose with facial and even pterygoid veins. (*d*) The ophthalmodural vein of Hyrtl (1859) is practically included under the more or less constant connection of the medicerebral vein and the sphenoid sinus. Occasionally this sinus or vein has a small anastomosis, through the lateral part of the orbital foramen, with the ophthalmic or other orbital vein. Evidently, the vena aberrans of Verga (1856) should be classed here. As a passage from the ophthalmic vein or cavernous sinus to the lateral sinus, Knott mentions one case (on right); or between ophthalmic vein and superpetrosal sinus, three instances (on left).

10. *The Emissary of the Foramen Rotundum* from the cavernous sinus, and accompanying the superior maxillary nerve as described by Nuhn, was twice seen by Knott (on right).

11. The medidural vein discharges largely through the *oval*, or *spinous, foramen*. Nuhn described a pair of veins which, after traversing the oval foramen, formed a plexus about the inferior maxillary nerve and terminated in the infratemporal veins. Knott found these veins on both sides in 18; two veins on right and one on left in 6, the reverse in 4; a single vein on each side in 11; no vein on one side in 5. Luschka and Trolard describe a vein, from the cavernous sinus, that receives dural veins from the anterior petrous surface and departs through the oval foramen; in this case the medidural emerges through the spinous foramen.

12. *Plexus s. Sinus Caroticus.*—Bell (1827) mentions a *vena sodalis arteriæ carotidis*, as an emissary from a petrous sinus, descending through the carotid canal. Rektorzik (1858) seems to have rediscovered this. A prolongation of the cavernous sinus into the carotid canal constitutes the sinus caroticus. This breaks up into a plexus of small veins about the artery, converging to one or more small trunks below, that may pass to the internal jugular. It may connect with 11 and 13. Knott was always able to find this communication, though the vessels varied much in size and number.

13. *Vena Medilacerata.*—Englisch is credited with having described (1863) a constant communication, outside the skull, between the cavernous sinus and the subpetrosal vein. As *inferior petro-occipital sinus*, Trolard independently described the same. "On the exterior base of the cranium a small vein occupies a groove extending between the two lacerated foramina. Its direction is laterocaudad. It inosculates with the cavernous sinus or carotid plexus, and with the pre-

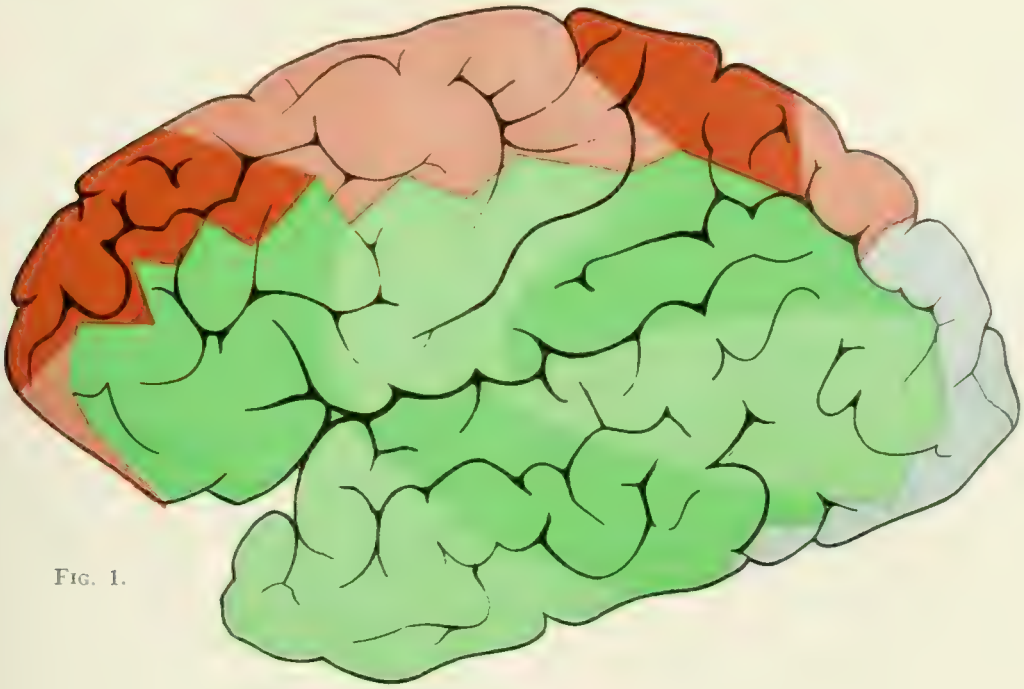

Fig. 1.

Fig. 2.

ARTERIAL DISTRIBUTION OVER CONVEXITY (FIG. 1), AND MESIAL SURFACE (FIG. 2): PRECEREBRAL IN BROWN: MEDICEREBRAL IN GREEN: POSTCEREBRAL IN BLUE. BRANCHES INDICATED BY SHADES OF THE PRIMARY COLOR.

condyloid confluens" (*vide supra, sub* 4). Knott found this in 14 out of 33 cases.

14. *Vena Subpetrosa*, from the subpetrosal sinus, through the premedian portion of the foramen postlacerum, to the jugular vein. Here it is separated—not rarely by bony lamina, thus forming the foramen anomalum of Gruber, 1869—by three nerve trunks from the jugular canal. From numerous investigations Gruber found that only rarely did this vein pass quite through the foramen before entering the jugular, and that then it first connected with the termination of the lateral sinus. However, in 8 out of 22 times Knott found that the vena subpetrosa ended at about the level of the lower margin of the jugular foramen, in 9 a little above, and in 5 a little below. It connects also with the precondyloid vein or confluens, and commonly receives the internal auditory veins.

15. *Sphenotemporal Emissary*, described by the writer (1897). More marked in the monkey, but traceable in forty-five of sixty human sphenoid alæ. A minor venous confluence connecting the sphenoidal sinus, the pretemporal diploic vein, the medidural vein, and externally the deep temporal veins.

To these may be added the following, of rare occurrence in the adult:

16. *Emissarium Temporale* (foramen jugulare spurium). This is held to be a relic of the primary jugular vein. When present, it proceeds from the prepetrosal sinus, perforates the temporal bone beneath the root of the zygomatic arch, emerges just behind the glenoid fossa at the edge of the porus acusticus externus, and ends in the external jugular system.

17. *Foramen Cæcum*, in fetal life a communication between the longitudinal sinus and the veins of the frontal sinus, ethmoid bone, and nose. Rarely, if ever, observed in the adult.

18. The very rare pathological venous blood tumors of the cranium (*vide* Mastin, *Journal of the American Medical Association*, 1886), arteriovenous aneurysms of the scalp, etc., occasionally communicate on the one hand with external veins of the head, on the other through openings in the bone usually with the long sinus.

19. Possibly a couple should be added from Hédon. Small rami accompany the olfactory bundles through the cribriform plate of the ethmoid, represented by the so-called Zuckerkandl's vein, of course connecting above with the vein of the olfactory bulb. "A vein leaves the aqueduct of Fallopius by the stylomastoid foramen to anastomose with the external jugular or postauricular (Sperino). It joins, according to Blandin, a small dural ramus traversing the hiatus of Fallopius."

Lymphatic System in the Brain.—There are no lymphatic glands in the cranial cavity; nor does the brain possess a system of independent lymphatics. Within the brain substance all the larger lymph passages accompany the blood-vessels as cylindrical enveloping spaces. These are at least twofold: (*a*) *Adventitial* spaces between media and adventitia, which latter are not closely bound together in the vessels of the central nervous system as in the remainder of the body; (*b*) *perivascular* spaces of His and Robin, connecting with the subpial or so-called epicerebral space. Their existence in normal tissues has been repeatedly disputed, and unquestionably their size is artificially much increased by the usual methods of preparation. Rossbach and Sehrwald, assert very positively the real existence of these spaces. They worked by Golgi's method, claiming that this marks the lymph, and thus the lymph spaces, rather than the ganglion cell and its processes.

The beginning of the lymph passages is to be sought in the very narrow spaces surrounding the ganglion cells—*pericellular spaces* (Obersteiner). To each of these latter spaces run, according to Rossbach and Sehrwald, many fine canals (rootlets), often coming a long distance through the albalis, and starting about vessels and from glial lymph spaces. These surround the protoplasmic cell processes. The efferents from these cell spaces pass along the apex process, branch, and empty into perivascular and superficial glial spaces, or directly into the epicerebral space. The lymph system of each ganglion cell has no direct anastomoses with that about any other such cell. They also describe a lymphatic plexus about the glia cells (*periglial space*), especially in the external cortical layer, and in the first subcortical albalis. These are often intermediary between the pericellular spaces and the perivascular spaces, into which latter and the epicerebral space they empty.

The results of Rossbach and Sehrwald, regarding lymphatics in the brain substance, are evidently discredited by Frommann (*Centbl. f. med. Wiss.*, 1888, pp. 881, 882). As regards the hypophysis, Pisenti and Viola (*ibid.*, 1890, pp. 451, 452) believe that certain structures observed by them represent lymph spaces. A cortical lymph-connective system has been studied by Bevan Lewis.

The lymphatics of the choroid plexus in the paracele unite (Arnold) to one trunk following Galen's vein. In the ependyma lymphatic networks have occasionally been observed.

The lymph passages collect in the pia to larger trunks, follow the course of the veins, and pass out, in part through the jugular foramen to superjugular glands, in part through the carotid canal to the deep cervical glands, in part beside the vertebral vessels to the infrajugular glands.

Little evidence of lymphatics in the myel is found by Kadyi. The perivascular spaces of His occur, but are likely of artificial origin. From the results of one injection he figures a network of voluminous canals running longitudinally beside the central canal, and that possibly represent a lymphatic system.

Serous Cavities, Cerebrospinal Fluid, etc.—Between dura and arachnoidea is the *subdural space*. In the normal condition this contains only a capillary layer of fluid. The dura has a system of lymphatics accompanying the blood capillaries, within their adventitia. Besides, in the endothelium of the dura independent lymphatic plexi and stomata have been described, presenting a communication with the subdural space, and conducting off the subdural fluid. Through the oval and spinous foramina pass (Arnold) lymphatics to the deep facial glands, probably coming from the dura.

The interstices of the pia, *i.e.* the somewhat broken room between arachnoid and pia proper, constitute the subarachnoidal space (*cavum subarachnoidale*). This is the retainer of the cerebrospinal (cephalorachidian) fluid. Although this fluid can pass back and forth between the corresponding cephalic and spinal spaces, it is no longer held that there is a continuous ebb and flow from one to the other at each respiratory movement and even pulsation. This space is exceedingly attenuated wherever the brain lies close to the skull, as over the convexity. At other points it forms lacuna-like pockets, termed by Key and Retzius cisternæ. Among these may be mentioned: *Cisterna magna* (*cerebello-oblongata*), where the arachnoid spreads across from the caudad border of the cerebellum to the oblongata; *cisternæ frontis* (*laterales et media*); *cisterna Sylvii;* and over the optic lobes the *cisterna ambiens*. The ventricles connect with these cavities (the celian fluid comes from the choroid plexuses—*vide Plate* XVIII., Figs. 3 and 4); the metepicele with the cisterna magna through the foramen Magendii and the aperturæ laterales; the paracele with the diacele per the foramen of Munro; and the diacele with the metepicele through the aqueduct. There is no canalis Bichati, formerly supposed to connect the paracele with the subdural space. Hence, while the celian and subarachnoid cavities are united,

neither has any direct connection with the subdural space. An indirect connection may be offered by the nasal lymph net, as this may be injected from the subdural as well as subarachnoidal space by way of perineural lymph passages about outgoing nerves. Another assumed indirect connection is by Pacchionian bodies and the sinuses. The experiments of Key and Retzius, confirmed by Kollmann (1880), seemed to show that the perforations of the dura—opposite venous spaces—by these bodies furnish one of the principal discharge paths for both subarachnoidal and subdural spaces. Certainly they do not usually attain any development until long after youth has passed. Further reasons in opposition are given by Adamkiewicz in his polemic (Eulenburg's "Real-Encyclopädie," 1886, art. "Gehirndruck") against Bergmann's theory of brain compression, and in favor of his own somewhat novel views. Material injected into the subarachnoidal space in animals traverses the supercervical and submaxillary glands. In man it can pass out in the optic sheath to the bulb, in the sheath of the facial and the acoustic as far as the internal auditory meatus—whence fracture of the petrous with tearing of the nerve sheath leads to oozing out of cerebrospinal fluid—and finally to the lymphatics in the nasal mucous membrane, the supposed path of meningeal infection from nasal sources.

The writer has shown that during the whole of fetal life in the human subject, there exist efferent passages for the cerebrospinal fluid along the larger nerve trunks from the spinal cord, notably those from the lumbar enlargement. After birth, however, these promptly close up, thus constituting the spinal arachnoidal sheath a blind sack. In the lower animals they are more persistent.

The subarachnoidal cisternæ protect the large basal vessels from compression, and in like manner the pericellular spaces shield the enclosed cell and its process from shock and distortion. Further, the perivascular channels protect the brain substance (His) in a more general way. WILLIAM BROWNING.

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Brain, Circulatory Disturbances in the.—ANEMIA.—Anemia of the brain is a condition resulting either from a reduction in volume or alteration in character of the cerebral blood supply. In either type the resulting symptoms are usually closely comparable except that when a reduction occurs in the volume of blood supplied to the brain, the expression is apt to be more sudden and much more severe.

We have no definite figures concerning the actual quantity of blood contained in the intracranial blood vessels, but Tschuewsky estimates that the blood-content at any instant is equal to four times the amount in one lower extremity. Sand states that the brain in man and the mammals can withstand a complete cessation of blood flow for twenty-five minutes, but that in many instances periods even as short as three minutes may result in its death.

In experimental anemia of the brain by ligation of both carotids and both vertebral arteries the results differ with the animal employed and this variation is probably due to differences in the richness of the anastomotic supply, which is called into service following the ligations. When the anastomoses, which are by way of the intercostal, ascending cervical and anterior spinal arteries which in turn feed the basilar, are sufficient to maintain the activity of the bulbar centers, the animal will survive the operation and will ultimately by development of the anastomotic pathways recover from its effects. Hill states that in none of the animals which he examined, does ligature of the carotids and vertebrals entirely cut off the brain from blood, but that in goats, horses, nearly all rabbits, and forty per cent.

of cats the anastomotic supply is too slight to maintain the activity of the bulbar centers when the ligature is suddenly applied, though the efficiency of the anastomosis can be greatly increased if the application is gradual. All dogs have survived the quadruple ligature and four have recovered completely after an initial period of paralysis and idiocy. Astley Cooper recorded the first of these experiments and the animal recovered and lived to be an excellent house dog. Kussmaul and Tenner tied off the cerebral supply and recorded spasms in ten to forty-five seconds. Immediately following the ligature the symptoms were loss of consciousness and volitional motion, then clonic spasms and cessation of respiration except for gasps at long intervals. Removal of the ligatures after two to three minutes immediately stopped the spasms and the brain showed the power of complete recovery. Jolly showed that washing out of the blood from the brain by physiological saline solution at ordinary arterial pressure also produced the typical spasms. Blocking of the venous return from the cranium, if complete, will give rise to similar symptoms, but their onset under these conditions is delayed. Hill gives the following description of one of his quadruple ligature experiments on the dog.

"December 4, 1895.—Two carotids and vertebrals tied.

"December 5.—The dog alternately sleeps and wanders round the room. When asleep powerful stimulations are required to rouse him. All his movements and tactile sensations are paresed. He stumbles into every object. His pupils react to light and the discs appeared pale with small arteries and large veins. Sounds are audible to it, as is evidenced by pricking up of the ear. Smell seems to be the most efficient sense. He continually keeps his nose on the ground, sniffing as he wanders about the room. Whenever meat is put into his mouth he eats reflexly, but does not notice pieces of meat that drop or hang out between his teeth. He drinks reflexly when his nose is put into water. He showed no concern at a cat, although the cat spat with rage; nor at a lighted match, nor at tobacco smoke blown into his face. He tries for many minutes to get through impossible objects—through crannies which are too small for him, bumps his head into every obstacle in the way, and finally drops asleep in front of such an obstacle. Sleep overtakes him at any moment during his perambulation. The scratching reflex did not seem to be exaggerated. Mouth temperature equals 36° C. Rectal temperature equals 39° C. Here was evidence of the deficiency of circulation in the head. Pulse 120, high tension. Respiration normal. Urine passed normally.

"December 6.—Much more susceptible to noise. Starts back on the firing of a match, and follows the light with his eyes like an infant. He shows, however, no fear of the light. There is still apparent no fear of a cat, for while the cat was hissing and trying to scratch, the dog calmly smelt round it. He showed difficulty in picking up and eating meat thrown before him. Walks more strongly.

"December 7.—Came across the room when called, and seemed pleased at notice. Passed feces.

"December 8.—Answered by movements to a call, and responds to patting. Seems frightened by a lighted match. Cannot localize a clip placed on his ear. Just as sleepy. Goes to sleep in any unnatural posture—on his back, or standing on his head, propped up against a cage. Quite uncertain how to jump down from a small height, gazed hesitatingly over the edge. Growls and turns to bite when irritated. All his acts appear reflex. Howled when meat was placed in his mouth, and then chewed and swallowed it.

"December 9.—Much more obtuse. Would not eat or drink. Fed with a tube. Growls at being interfered with.

"December 10.—Ate meat when placed in his mouth. Very little power of mastication. I injected glycerin into the rectum, and the dog ran round and round the room many times, then had a motion, and straightway fell asleep; scarcely feels and does not localize a clip placed on the ear. When a string was tied on his tail he wound himself round and round a post and then tried to get under his own tail. After this date the dog rapidly recovered.

"On December 14 he was shown to the Physiological Society, and seemed practically a normal dog, save for some weakness and hesitation in jumping from heights.

"On December 16 the dog was killed, the ligatures verified. The anastomotic arteries were found to be the intercostals and ascending cervicals, and mainly the branches of the superior intercostals. These last had become dilated up to the size of the vertebrals and supplied the basilar arteries, and thence the whole brain."

Considerable discussion has arisen over the question of an independent vasomotor nerve supply to the intracranial vessels. Hill reviewing the situation in 1895 came to the conclusion that there was no evidence of the existence of vasomotor nerves or local vasomotor control of the cerebral supply and that the whole regulation of the intracranial circulation was by means of the reciprocal relations of the splanchnic field, *i.e.* that vasoconstriction in the splanchnic area results in forcing a larger volume of blood into the general circulation and thus indirectly increasing the cerebral supply and, *vice versa*, that splanchnic dilatation by withdrawing blood from the circulation will tend to diminish it. He also concludes that there is no evidence of the causation of cerebral anemia by spasm of the cerebral arterioles. These conclusions embody the opinion of the majority of the physiologists, but the presence of nerve fibrillæ accompanying the cerebral vessels has been demonstrated by histological methods by a number of investigators—notably Huber, who found that both pial and dural vessels were accompanied by nerve fibrillæ of two types—a slender non-medullated plexus, similar in all respects to the vasomotor supply of vessels in other parts of the body, and larger medullated fibers which are interpreted as sensory fibers. Kölliker describes nerve fibers on the branches of the circle of Willis which branch to follow all of the vessels of the pia and states that he has followed them on arteries of 90μ and smaller into the substance of the brain. Obersteiner believes that the vasomotor nerves of the brain are more easily fatigued and fail to respond at times when other vasomotor nerves of the body still react and suggests this as a part at least of the reason why physiological experiments have given negative results.

In view of the demonstration of fibrillæ on the cerebral vessels which in all respects accord with those of arterial plexuses elsewhere, one feels inclined to accept the conclusion of Testus that "they are here as in other parts of the body regulators of the circulation." On the other hand, however, many of the experiments of Hill and others are equally impressive in suggesting the importance of the splanchnic area. It seems reasonable therefore to conclude that the condition of the vessels in the splanchnic field may play a very important part in the regulation of the gross changes in blood volume within the cranium, but that the finer variations (too fine possibly to be recorded by the methods employed) may be controlled by active vasoconstriction and vasodilatation under command of vasomotor nerves. This may apply equally to the intracranial circulation as a whole and to the variations of blood volume in various areas of the cerebral supply.

Ligation of the carotid arteries is occasionally indicated in man by aneurysm, injury, etc., and if carried out suddenly Jacksonian convulsions or tran-

silent hemiplegia may occur. Shiff and Hill each report the production in themselves of spasms on the opposite side of the body by compression of one carotid. This bespeaks a tardy or incomplete compensation by the circle of Willis. An interesting light is thrown on this question by the experimental work of Kramer, who found that in dogs and monkeys methylene blue solution injected into one carotid, if the operation was carried out carefully so as not to raise the intra-arterial pressure of that side, made its way to only a very limited extent to the opposite hemicerebrum. Variations in the size of the communicating branches of the circle of Willis are frequent and would play an important part in individual reaction to carotid ligation. The causes of anemia of the brain through considered here as they pertain to anemia in general.

The *causes* of acute anemia of the brain as a whole may be stated as follows:

1. Occlusion of the whole cerebral arterial supply by ligature, embolism or compression. This is largely an experimental condition and needs no further elaboration.

2. Occlusion of all the cerebral venous sinuses. Hermann and Esher by ligation of the superior vena cava and azygos veins and obliteration by cautery of the veins of the spinal cord and vertebral canal obtained the same sequence of symptoms as are seen in ligation of the arterial supply. Ferrari obtained a similar result by the injection of wax into the sinuses.

3. Hemorrhage. The sudden withdrawal of a large quantity of blood from the general circulation may result in a reduction of the volume sent to the brain. This must, however, be a sudden withdrawal and the quantity of blood must be large, as the vasomotor mechanism is active in readjusting the distribution. The effect of this type of reduction in volume will be aggravated by the erect posture and alleviated if the head be on as low or a lower level than the heart when the influence of gravity is less directly exerted against the cerebral blood stream.

4. Sudden vasomotor paralysis plus the effect of gravity. Hill has shown that when the vasomotor center of a dog has been destroyed by pithing, gravity plays a most important part. Thus, in such a dog a vertical position with the head up produces syncope, which immediately disappears on reversal. In the monkey (as is probably also true in man) the compensation for the effects of gravity is much greater than in those animals which are not upright.

In close relation with this cause is that of the sudden withdrawal of blood to other parts of the body, as for instance after violent labor with incomplete contraction of the uterus but without much external bleeding, syncope may result from the amount of blood withheld from the general circulation in the suddenly released uterine sinuses. The symptoms of collapse following aspiration of large serous exudates from the body cavities due to the sudden release of pressure on large vascular fields are probably also of this nature in some cases.

Chloroform poisoning may result in a vasomotor paralysis without cardiac involvement, giving rise to symptoms of collapse which may be relieved by pressure on the abdomen by giving rise to mechanical vasoconstriction, thus returning to the general circulation some of the blood which had drained into the splanchnic field.

5. A sudden increase of intracranial tension. The brain substance is relatively incompressible and the amount of cerebrospinal fluid which is present in the cranial cavity in physiological conditions is small, so that large changes in volume within the rigid cranium are dependent largely on the blood volume. If now there be a sudden increase in tension, the smaller capillaries will be obliterated until such time as readjustment through venous outflow can occur. This consideration is of interest in experiment, where it is found that dangerous symptoms do not occur through gradual injection of foreign material, until the arterial pressure is reached, thus suggesting that the symptoms themselves are the result of anemia from interference with the inflow of arterial blood. When, however, the injection is rapid the symptoms follow a minor increase of pressure. In cerebral hemorrhage, the influx of blood into the brain is at the arterial pressure and hence capable of obliterating capillaries, and here again many of the major symptoms may be due to the effects of anemia, brought about by the pressure, rather than to the pressure itself.

6. Heart disease. In patients suffering with insufficient action of the heart any sudden increase of exertion may give rise to syncopal attacks. This is especially true in aortic regurgitation and in fatty or fibrous myocarditis, and is also frequently seen in convalescents from acute febrile diseases.

7. Spasm of the cerebral arteries. This is a cause which has long received credence as one of importance in the explanation of syncope and even in epilepsy. The negative evidence adduced by the physiologists, while not excluding this factor, renders it improbable that it is a prominent one.

8. As a miscellaneous group may be mentioned the syncopal attacks, which probably result from a cerebral anemia following emotional and mental excitement in delicate or neurotic persons, intestinal disturbances, especially when associated with abdominal pain, and the immediate syncope and collapse which occur in gastric and intestinal perforation. Both of these conditions probably bear a close relation to splanchnic vasomotor paralysis and sudden withdrawal of blood from the general circulation into the splanchnic vessels.

Symptomatology.—In cases of acute cerebral anemia the onset of the symptoms varies somewhat. In many cases loss of consciousness is the first indication. In more gradual ones the first symptoms are a feeling of lightness in the head and a slight difficulty in breathing frequently followed by tinnitus aurium, dizziness, slight nausea or even vomiting, uncertain equilibrium and generally a marked reduction in the acuity of perception of sensory impressions, vision is blurred and audition indistinct. Objectively the face is pale, the pupils at first contract and then dilate, the skin is pale, cold, and moist, and the pulse becomes slow and small in volume.

In cases of severe sudden loss of blood in previously healthy patients, convulsions may occur. These may be Jacksonian in type or general. Marshal Hall states that in blood letting convulsions stand next to syncope in order of frequence. Complete paralysis does not occur, though a transient hemiparesis or hemiplegia may follow ligation of one carotid artery. Curiously enough convulsions rarely follow hemorrhage, even when sudden and severe, in patients who are much debilitated.

The symptoms following experimental cerebral anemia have been tabulated by Hill as follows: 1. Loss of consciousness and convulsions. 2. Respiratory spasm. 3. Slow heart and rise of blood pressure with cessation of respiration. 4. Fall of blood pressure, acceleration of the heart, and death. He states that the fatal symptoms arise only when the bulbar circulation ceases, and that when the anemia is slow in advancing it fails to produce the excitatory symptoms, and calls attention to the similarity to the symptoms of asphyxia.

Diagnosis.—The diagnosis of anemia of the brain depends on the general symptoms outlined. Attention should be directed, however, toward the question of severe heart lesions or general anemic states.

Prognosis.—The prognosis in simple syncopal attacks is good, although fatal results occasionally occur. It is a trifle less favorable in cases following severe hemorrhage, while as a result of cardiac disease, syncope serves as an index of a weakened compensatory activity which offers a serious outlook.

Treatment.—In simple syncope a horizontal position, fresh air, and simple stimulant inhalants such as the familiar smelling salts are usually efficacious. In more severe attacks cold water or the electric brush externally, with coffee, alcohol, or ether internally are indicated. Tight bandaging of the abdomen (preferably) or of the limbs is frequently of value by returning blood to the general circulation.

When complicating heart disease or general anemia, the treatment must be directed to these conditions.

Hyperemia.—Hyperemia of the brain is usually considered under the two subdivisions of active or arterial hyperemia and passive or venous congestion. Hill has pointed out that any marked increase of arterial inflow into the cranial cavity can take place only at the expense of the capillary or venous blood content as the brain substance is incompressible, the cranial cavity rigid, and the amount of cerebrospinal fluid under normal physiological conditions is so small as to be practically negligible. A sudden marked increase on the arterial side will thus result in either the temporary obliteration of capillary areas where the intracapillary pressure is lower, or by compression of the sinuses at their points of outflow, thus tending to raise the whole intracranial pressure to that of the arterial tree. In either event the result will be a more or less widespread anemia (either by expression or by stasis) and the symptoms arising will be closely comparable, if not identical, with those of cerebral anemia. Hill further states that in all physiological conditions the volume of the blood in the brain is practically constant and that rise of arterial pressure results in acceleration of the flow without notable increase in volume. A consideration of physical conditions under which the cerebral circulation is at work, would lead to the conclusion that this must be equally true of pathological states except in those cases where the increase of blood flow is so sudden in onset that sufficient time is not available for a compensatory increase of venous outflow, which will result in the increased intracranial tension with the results outlined above. In cases with persistently high arterial tension, therefore, the evidence warrants us in assuming that the effect on the cerebral circulation is that of an acceleration of flow rather than of an augmentation of volume.

Venous congestion, on the other hand, is of greater pathological importance. Intracranial pressure can be shown to vary directly and absolutely with venous pressure while it varies only proportionately with arterial pressure. Ferrari injected wax into the venous sinuses and found that the symptoms occurring on complete obstruction were entirely comparable to those occurring in cerebral anemia. Hermann and Esher obtained a similar result by venous ligation and cautery. The only difference observed by these authors between this operation and ligation of the arterial supply was that of the time of onset of the convulsive seizure, which in the case of the veins was double that of the arterial operation. They also found that ligation of the superior vena cava and azygos veins had no effect unless supported by obliteration of the veins of the spinal cord and vertebral column, thus indicating the freedom of the craniovertebral anastomosis.

At autopsy the findings with regard to the cerebral blood volume are inconstant and a review of the factors will tend to shed some light on the question. In acute inflammatory reactions within the cranium, such as acute meningitis or acute encephalitis, the widespread capillary engorgement of both the vessels of the meninges and the brain itself are self-evident. This of course is a local inflammatory reaction. It is probable that the intense congestion of the brain found in chronic alcoholics and opium eaters is of like nature, *i.e.* a reaction to the toxic or inflammatory action. Active general hyperemia, however, as well as venous congestion are dependent on conditions which are varied during the agonal state and entirely altered after death. Thus if the agonal conditions are such as to result in a marked withdrawal of vasomotor compensation before the cessation of the heart's beat, the relaxation of the large vascular fields in the trunk and extremities and especially that of the splanchnic area will result in such a marked withdrawal of blood from the general circulation that the heart may not receive a supply sufficient to engorge the cerebral vessels, even though they are in a receptive condition. Conversely, if the vasomotor activity is continued well into the agonal period, the tendency will be toward the production of a congestion of the brain which may be demonstrable at autopsy. Conditions of posture after death, when all the vessels are relaxed and the tendency of the blood is to seek its gravity level, may also prominently affect the post-mortem findings.

Symptomatology.—We know nothing of the clinical symptoms of active hyperemia of the brain. In acute experimental venous congestion the symptoms are exactly comparable to those of cerebral anemia. Venous stasis of the brain gives rise to a sense of fulness in the head, slight dizziness, flashes before the eyes, and occasionally to syncope. Though often ascribed to cerebral congestion, there is large question whether mental disorders, delirium, paresthesias, and motor disturbances are not results of a cause common to the circulatory disturbance and in no way dependent on the latter, much as we explain delirium tremens on the basis of the alcohol rather than of the cerebral congestion which accompanies it.

Treatment.—Venous congestion is best combated by rest, removal of any constricting clothing from the neck or abdomen, and moderate purgation.

Cerebral Embolism and Thrombosis.—Embolism and thrombosis of the cerebral arteries both give rise to a similar group of symptoms. When the condition is presaged by a series of prodromes, the probabilities may be said to favor the diagnosis of thrombosis rather than embolism, though the growth of a propagating thrombus from a small embolus may mask the picture. Embolism of the cerebral veins and sinuses, however, yields a rather different picture, and while differential diagnosis may be difficult or even impossible, the symptoms warrant separate treatment.

Cerebral *emboli* may arise from any of the major sources of arterial embolism except those pertaining to the aorta below the origin of the innominate and carotid arteries. By far the most common origin is that of valvular endocarditis of the left heart. Mural endocarditis either primary or dependent on an underlying myocarditis of the left auricle or ventricle is another frequent source of cerebral emboli. Saveliew states that eighty-nine per cent. of all cases of cerebral embolism are associated with heart disease. Gangrenous or thrombotic processes in the lungs with the advent of free particles into the returning pulmonary blood may also give rise to emboli which may find their way into the cerebral vessels. This path of translation is also of considerable importance in the origin of cerebral abscesses, as the embolic material in many of these cases is septic. The writer has seen on the autopsy table one such case of cerebral abscess in a child, where the focus of origin was without much doubt due to a septic embolus from a purulent peribronchial process, set up and kept active by a large black-headed pin which had been swallowed six years before the onset of the cerebral symptoms (reported by Beebe). Atheromatous degeneration of the ascending aorta may also serve as an origin of emboli, through the formation of thrombi, small portions of which are whipped off into the blood stream. Rarely, as in Cohnheim's case, the embolus may arise in the veins of the trunk and find its way through a patent foramen ovale. The foramen ovale may be shown

to be patent in a considerable number of hearts (one in three, Lewandowsky) though in the majority the opening is well covered by endocardial flaps. The right heart appears to be less susceptible to the causes underlying endocarditis and thrombosis, and this coupled with the infrequency of a foramen ovale, which will allow of ready transmission of blood from one side to the other, places this possible source among the improbable ones.

The explanation of cases of sudden death or paralysis occurring during aspiration of the pleural cavities on the basis of embolism from the pulmonary veins, has been in part substantiated by autopsy findings, but in many cases such emboli have not been discovered even after painstaking search, and it is probable that while embolism may be the active factor in some of these cases, the anemia produced by the sudden reopening of a large vascular field is also an important cause, especially in those cases where the paralyses are transient.

The embolus itself is usually made up of particles of fibrin containing leucocytes and erythrocytes, though occasionally bits of ulcerated valves or atheromatous detritus are included.

The course of the embolus and in consequence the group of localizing symptoms is inconstant. There are, however, certain sites of predilection and chief of these is the middle cerebral artery. Von Monakow claims that this artery is involved in eighty per cent. of cases. Gelpcke states that the left middle cerebral is more frequently involved than the right in the proportion of 6 to 5. The occurrence in the middle cerebral is explained on the ground that this vessel is a more direct continuation of the internal carotid than the other cerebral vessels, while the slight preponderance of the left over the right is explained likewise because it forms a more direct path from the heart.

Saveliev states that cerebral embolism is more frequent in women than men in the proportion of 8 to 7. Osler explains this on the basis of the greater frequency of mitral endocarditis in women.

With regard to the age of occurrence Saveliew has given the following distribution by decades in 134 cases:

1–10 years...	4 cases.	41–50 years .....25 cases.	
11–20 years...	17 cases.	51–60 years.....26 cases.	
21–30 years.....33 cases.		Over 60 years.... 6 cases.	
31–40 years .....25 cases.		Total.....134 cases.	

Capillary emboli need not be described here, but mention might be made of the fat embolism following crushing bone injuries and occasionally after orthopedic operations. Tumor cells may also be found forming capillary emboli or larger bits may give rise to areas of softening as described by Winkler. Liver cells have been reported in the cerebral capillaries in acute yellow atrophy of the liver, and occasionally in fulminant cases of malaria, capillary pigment emboli are found.

Cerebral arterial *thrombosis* may arise from an embolus, or from lesions of the vessel walls, in aneurysms both gross and miliary and occasionally as a result of abnormality in the blood itself.

When an embolus finds lodgment, it quite frequently serves as a point of origin for a propagating thrombus. In the case of a rider embolus, this propagation may serve greatly to increase the interference with the amount of blood passing into either branch of the bifurcation. When an embolus is stopped only when it reaches a point of too small caliber for its passage, it serves to block completely the vessel and the clotting which takes place in peripheral portions will not give rise to further disturbance. There is also, however, usually clotting in the proximal portion of the vessel back as far as the first branch, and extension or fragmentation of this clot may serve to cut off additional areas.

Endarteritis of the cerebral vessels may give origin to thrombi. This is especially true of areas of atheromatous softening. It is also widely stated that thrombosis is apt to follow syphilitic endarteritis. The problem here is somewhat complicated by the similarity both in clinical course and ultimate anatomical findings of thrombosis and syphilitic obliterative endarteritis.

The obliteration of an aneurysmal sac by thrombosis may be the starting-point from which occlusion of the diseased vessel may take place.

Certain conditions of the blood seem to favor thrombosis without local vascular lesion. This type is of much more frequent occurrence in the veins than in the arteries and makes up the group of primary sinus thromboses (*q.v.*). It does occur, however, also in the arteries in the cachexia of carcinoma and marasmus and in association with the infectious diseases.

Pathological Anatomy.—The majority of the vessels of the substance of the brain are described as terminal arteries, while even in the pial vessels, the anastomoses are slight. Observations on the extent of softening in various cases of plugging of arteries suggest that there is wide individual variation in the extent of the anastomoses between various branches, but that if the vessel involved be a large one, there will always be a certain proportion of its distribution which will not receive blood supply in sufficient amount to maintain its integrity, and in general the statement that the deep vessels are terminal arteries is warranted. The variation in the anastomoses of the pial and cortical vessels probably accounts for the differences observable in the resultant lesions. Infarcts of the brain as a rule are of the pale or anemic variety, though the capillaries may be filled by reflux of venous blood (Cohnheim) or from adjacent capillary fields (Litten). This refilling may give rise to a red or hemorrhagic infarct and this type is seen almost exclusively in the cortex. In large areas of recent infarction, involving both cortex and subjacent white matter, one often sees the two types well contrasted, the hemorrhagic infarct more or less sharply localized in the cortex while the white matter is anemic.

Following this acute stage the necrotic process begins. The analogy offered by experimental anemia of the brain suggests that probably a functional loss results within a few seconds after the plugging and that death of the nerve elements occurs within twenty-five minutes thereafter, while the liquefaction probably does not begin actively until the second or third day. All of these periods will depend of course very largely on the richness of the anastomotic supply. The nerve cells and fibers of the involved area undergo fatty degeneration and finally liquefaction and absorption, leaving the so-called cyst of softening which will show color varying from slightly yellowish to a decided brown, depending on the amount of blood pigment which is taken up by the wall of the cyst. Yellow areas of softening—the *placques jaunes*—are not uncommon in elderly persons and are seen as areas of one to two centimeters in diameter, sometimes angular in shape and filled with grumous yellow material or clear serous fluid.

Symptomatology.—Embolism of the cerebral vessels gives rise usually to a group of primary symptoms which are the counterpart of those of cerebral hemorrhage, and a differential diagnosis is often impossible. The attack is usually sudden and without prodromes, and varies in severity from the deep coma of a typical apoplectic stroke to a short loss of consciousness, or even to a transient vertigo and confusion. General or unilateral convulsions may occur. Usually in embolism, however, the characteristic rise of temperature which follows shortly after an attack of cerebral hemorrhage is wanting. There is usually a slight rise of temperature, but it is short-lived and variable, though in fatal cases a marked and persistent rise may occur.

Thrombosis of the cerebral arteries, while giving rise to a very similar series of symptoms, is much more apt to show prodromes. Abrupt loss of consciousness is much less common than in embolism and the patient has often previously complained for some time of headache, vertigo, tingling in the extremities or weakness of one side or dysarthria. Finally if the paralysis appears, it is apt to be slowly progressive and is often incomplete or variable.

No attempt will be made here to enumerate the various localizing symptoms, but a general review of the more common sites with their results may be given. As indicated above, in the majority of cases embolism affects one of the middle cerebral arteries—the left somewhat more frequently than the right. If the embolus lodges before the point of origin of the deep branches is reached, a permanent complete hemiplegia will result from softening of the internal capsule in the neighborhood of the basal ganglia. If the obstruction takes place, however, beyond the origin of these vessels, the paralysis is more apt to be transient and the involvement of the face and arm will be greater than that in the leg. When left sided, the paralysis is apt to be accompanied by aphasia which is usually of the subcortical motor type (Marie's anarthria) though by involvement of the left superior temporal branches of the Sylvian artery, a word deafness and sensory aphasia may result. If the branches to the angular and supramarginal gyri be occluded on the left side, alexia or the so-called visual aphasia will follow. Disturbances of tactile sensation may follow lesions involving the postcentral gyrus, but these as a rule do not include a total hemianesthesia, as it seems probable that the lower centers (*i.e.* thalamus, etc.) are, to a limited extent at least, capable of perception of tactile impressions though they do not serve to localize them accurately.

When the posterior cerebral is involved, the chief symptoms are referable to the occipital lobe, *i.e.* hemianopsia and alexia, though hemianesthesia may result from involvement of the posterior parts of the internal capsule and of the optic thalamus.

Following involvement of the anterior cerebral, the localizing symptoms may be few. This artery usually feeds the paracentral lobules and a part of the upper portions of the precentral gyrus. Monoplegia of the leg may result though usually branches of the middle cerebral are sufficient to keep up the circulation in this field. Intellectual disturbances, emotional instability, hebetude, and somnolence are conditions which may result.

Emboli are probably much less frequent than thrombi in the vertebrals and basilar, but the resulting symptoms of either are characteristic. Paralysis, either unilateral or bilateral, may occur through damage to the pyramidal tracts. More frequent is the occurrence of crossed paralysis. In this condition the paralysis of the extremities is of the type associated with lesions of the pyramidal tract (corticospinal neurone), while the paralysis in the face, which is on the opposite side of the body from that in the extremities, is of the peripheral type (spinomuscular neurone) due to the destruction of the nuclei of origin of the involved nerves below the point of crossing of their respective cortical paths.

Embolism or thrombosis in the internal carotid is variable in its results. There may be no paralysis or a transient or permanent hemiplegia. These variations depend on the size of the anastomoses in the circle of Willis and the ease with which collateral circulation may be established through them. When the blocking is within the skull, the thrombosis usually extends to the branches of the carotid resulting in hemiplegia, coma, and usually death.

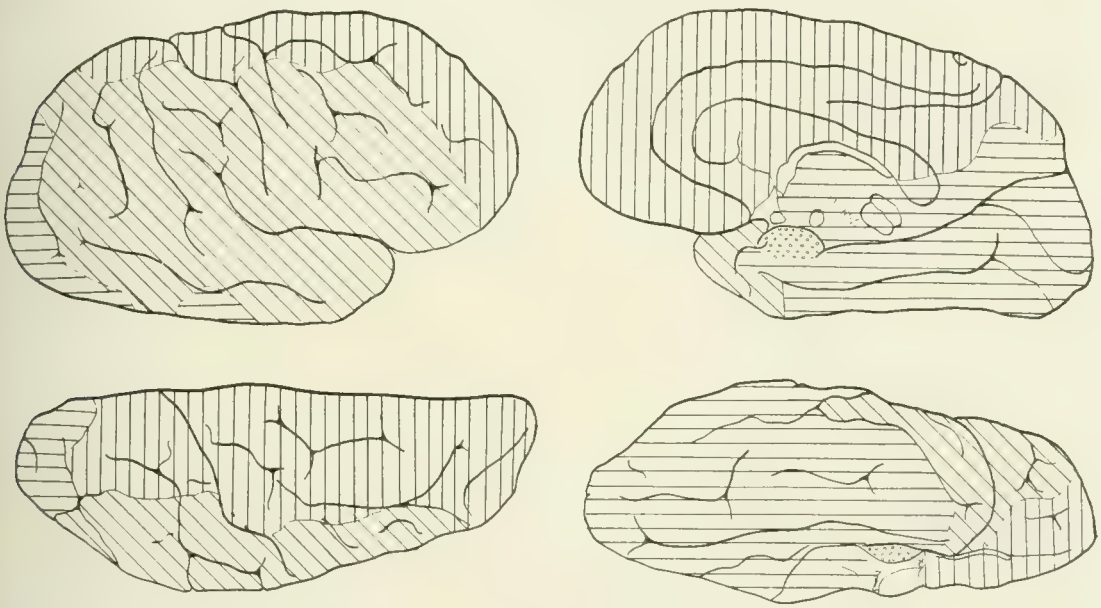

Fig. 1007.—Distribution of the Major Cerebral Arteries. Vertical lining represents field of supply of the anterior cerebral; horizontal, that of the posterior cerebral; diagonal, that of the middle cerebral. (After Beevor from Lewandowsky.)

The accompanying chart (Fig. 1007) shows the usual distribution of the three major cerebral vessels. The possibility of wide individual variations both in distribution and richness of anastomosis must be kept in mind.

The secondary symptoms of cerebral embolism are again like those of cerebral hemorrhage with a marked exception in their course. In cases of either which do not succumb to the primary disturbance, a certain degree of amelioration is to be expected. Thus in a hemiplegia from either cause, the extent of the paralysis immediately apparent will be much greater than the residual. In embolic hemiplegia, however, the recovery is more rapid than in that following hemorrhage. This is probably due to the fact that the disturbance of function in the area immediately sur-

rounding an infarct is more readily alleviated through the more rapid absorption of the products of degeneration than in a case with formation of clot. In general, it may be said that paralysis remaining at the end of two weeks after the onset of cerebral embolism will be permanent, while in hemorrhage gradual improvement may be expected for a considerable period.

Following the period of partial recovery, the paralyzed limb becomes spastic or contractures may occur. Atrophy is as a rule slow and of minor grade. The residual paralysis is rarely of even distribution throughout the affected side. Thus in one case the leg will bear the brunt of the permanent disability, while the remaining paralysis in the arm and face will be of lesser grade or the arm may show the greater involvement, while the leg and face show less permanent paralysis. Facial residuals are much more infrequent than those in the extremities. The arm shows the greatest tendency to contracture resulting in a flexion of elbow, wrist, and fingers, which becomes permanent. The spacticity of the leg occurs usually without much contracture and makes it possible for the patient to get about through movements of the bilaterally controlled hip and trunk muscles. The leg is stiffened and acquires a characteristic drag, and the movement is entirely or almost entirely through revolution of the pelvis about the axis of the sound side. The condition at this stage is that of a unilateral pyramidal tract sclerosis and the deep reflexes on the paralyzed side are increased through the withdrawal of the inhibitory activity of the pyramidal tract impulses. Babinski's sign and ankle-clonus are usually present. Hemianesthesia or irregular anesthesias may occur.

Cerebral arterial thrombosis shows a tendency toward involvement of two of the major cerebral vessels as contrasted with cerebral embolism in which the vessel affected is usually single. In some of these cases a direct communication by way of the branches of the circle of Willis seems probable, for instance, in bilateral involvement of the posterior cerebrals or in thrombosis of posterior and middle cerebrals of the same side. On the other hand, Von Monakow has pointed out that thrombosis of the posterior cerebral of one side is frequently associated with a like disturbance in one of the branches of the opposite middle cerebral.

Diagnosis.—The differential diagnosis between cerebral embolism or thrombosis and cerebral hemorrhage is, as can be seen from the foregoing account of the symptoms, often impossible. The prodromes and more slowly progressive character of the onset often will serve to distinguish thrombosis. The occurrence of a sudden right-sided hemipelgia and aphasia in persons with no previous signs of disease is sometimes said to warrant the diagnosis of cerebral embolism, but a left internal capsule hemorrhage may give rise to the same syndrome. As may be seen from the above table from Savelièw cerebral embolism is not characteristically a disease of advancing years. Hemorrhage, on the other hand, is definitely so and the occurrence of apoplectiform seizures in young patients in whom syphilitic disease of the vessels can be readily excluded would suggest the diagnosis of cerebral embolism. The presence of a demonstrable heart lesion is likewise strong evidence in favor of an embolic disturbance, though most cases of cerebral hemorrhage rest also on a basis of widespread cardiovascular disease. The irregular temperature reaction of the few days following the stroke may aid in the diagnosis, while rapid clearing up of the initial paralysis also suggests embolism rather than hemorrhage. Rapid and increasing rise of blood pressure is said to be an accompaniment of hemorrhage.

Prognosis.—The following table quoted from Jones in Lewandowsky's Handbuch suggests the relative severity of the three conditions with regard to life.

Death occurs from	Within 24 hours.	By end of first week.	By end of first month.
Cerebral hemorrhage..	37.7%	72.5%	86.2%
Ventricular hemorrhage	60.0%	90.0%	
Cerebral thrombosis...	8.7%	30.4%	60.8%
Cerebral embolism....	0.0%	30.7%	30.7%

In the individual the prognosis will depend largely on the concurrent conditions, *i.e.* heart disease, chronic nephritis, alcoholism, diabetes, etc. In young patients recovery from the attack is the rule and a certain amount of improvement in the paralysis or aphasia, etc., is to be expected, but the warning should be given that some permanent disturbance is almost certain and that recurrent attacks are possible. Rapid and continuous rise in temperature, respiratory disturbances, and prolonged coma are danger signals. In embolism or thrombosis of the vertebrals or basilar, giving rise to definite bulbar symptoms, death may be expected.

Treatment.—Treatment of cerebral embolism and thrombosis is unsatisfactory and in the main symptomatic. The patient should be placed in bed with the head slightly elevated, with all constricting clothing removed from the neck, and should be kept absolutely quiet. Venesection or depletion by purgatives is contraindicated, but the bowels should be opened. Small doses of digitalis may be required if the heart's action is feeble and irregular. When syphilis is an active factor potassium iodide, from twenty to thirty grains or more daily, may be given with the addition of mercurial inunctions if the case is of recent infection. There is grave doubt whether the use of salvarsan should be attempted in the presence of cerebral involvement, but it may be considered as a last resort.

For the treatment of the residual paralysis little can be done. The recovery of power is limited by the extent of the lesion, but passive motions, gentle massage toward the body and faradic stimulation may all be applied after the lapse of ten days to two weeks with the intention of preventing too great deformity or to alleviate contractures after their occurrence.

Thrombosis of the Cerebral Veins and Sinuses.—This condition may be divided for discussion into two classes—primary and secondary.

Primary sinus thrombosis is rare. It occurs typically in marasmus or during diarrhea in infants, in chlorosis and anemia, and in the terminal cachexia of tuberculosis, carcinoma, etc. As additional etiological factors, the acute infectious diseases, typhoid fever, syphilis, and trauma may be mentioned. In many of these conditions there is doubt whether or not bacterial infection does not play a prominent part. In chlorosis and anemia as in the marantic thrombi, however, it is probable that blood conditions are the chief factor and in all, thrombi may occur without relation to adjacent foci of infection and hence may be properly termed primary.

The site of election seems to be the superior longitudinal sinus (seventy per cent.—Vaitl), but any of the sinuses or veins may be implicated, or several may be involved at once. When a vein or sinus without ready collateral anastomosis becomes thrombosed, widespread red softening and massive bleeding occur first into the brain substance and finally into the ventricle.

Symptomatology.—The symptoms of primary or autochthonous thrombosis are very variable. Fever may or may not be present, or it may be present only at the onset. Occasionally it may be high, more frequently the temperature is subnormal. Local symptoms are not often present but when massive red softening attacks isolated areas, symptoms may

arise which can in no way be differentiated from those following arterial thrombosis. Among the general symptoms may be mentioned choked disc, headache, mental dulness, vomiting, delirious conditions, and motor unrest. Thrombosis may occur, however, without any symptoms of sufficient severity to attract attention. This is particularly true of thrombosis of the superior longitudinal sinus which may be unsuspected until revealed at autopsy. The experiments of Hermann and Esher quoted above show a parallel absence of symptoms in experimental partial blocking of the cerebral venous return. Exophthalmos may be a prominent symptom and Lewandowsky states that choked disc may be practically the only symptom of the sinus thrombosis, and the occurrence of choked disc in the course of chlorosis should therefore always suggest the possibility of thrombosis.

Prognosis.—The prognosis is as a rule very unfavorable when the case has reached the point where a diagnosis is made, but cases of recovery in chlorotic girls with choked disc, etc., are recorded. (Hawthorne *et al*).

Treatment.—No satisfactory treatment of the thrombosis is available. The patient should remain in bed in absolute quiet, with the neck unrestricted and further treatment should be aimed at the underlying conditions.

Secondary or purulent thrombosis is due to an extension of a septic process from some adjacent focus. In eighty per cent. of cases the source is from otitis media with or without complicating mastoiditis, though it seems to be less frequent from the mastoid than from the middle ear. Its path may be directly through the affected bones or it may pass in by way of emissary or tributary veins. Other sources are facial erysipelas, carbuncle, suppurating disease of the accessory nasal sinuses, parotitis, tuberculous caries of any portion of the cranium and fracture of the skull. The infected thrombus may give rise to septicemia or pyemia or it may become walled off and form an abscess, or in very rare cases may go on to organization and spontaneous cure.

Symptomatology.—The greater part of the symptoms are those associated with the local focus of suppuration plus the sudden addition of signs of septicemia or pyemia. Localizing symptoms and severe disturbances of consciousness are rare. Thrombosis of the lateral sinus often results in painful edema of the mastoid region, probably resultant on thrombophlebitis of the mastoid emissary veins. When continued down into the jugular vein the clot can be recognized by palpation. When the sinus cavernosus is attacked, edema of the eyelids, retrobulbar edema with exophthalmos and optic neuritis may occur. In disease of the longitudinal sinus edema of the parietal region, edema of the face, and epistaxis are occasional though not constant symptoms. Paralysis of certain areas of nerve supply may result from extension of a periphlebitis to the adjacent nerves in their passage through the bony foramina of the skull. Thus the vagus, spinal accessory, and glossopharyngeus nerves may be involved in the jugular foramen and the oculomotor, patheticus, and abducens may be affected at the point of relation with the cavernous sinus.

Diagnosis.—The diagnosis of septic sinus thrombosis depends largely on the association of local foci of suppuration with the signs of septicemia and pyemia, as the special symptoms are by no means constant in appearance. The appearance of pulmonary or other distant pyemic symptoms is an important clue.

Prognosis.—Septic thrombophlebitis within the cranium rarely heals spontaneously. In the great majority of cases death occurs from septicemia, pyemia, pyemic metastases (especially to the lungs), meningitis, brain abscess, or sinus hemorrhage. Lung involvement gives a distinctly unfavorable outlook.

Treatment.—Surgical intervention offers the best hope of relief. Especially is this true of septic thrombosis of the lateral sinus which, after ligation of the jugular vein, can be readily opened and drained. In the event of operation the prognosis depends on the resistance of the individual, the severity of the infection, and the freedom of the drainage.

Softening of the Brain.—Softening of the brain had already been in part described under the heading of embolism and thrombosis, but certain other conditions are of sufficient interest and importance to warrant separate treatment.

General Encephalomalacia.—At the autopsy table one frequently finds a condition of general encephalomalacia—characterized by a general reduction in firmness of the brain mass not unlike the result of postmortem autolysis. Its occurrence, however, in brains removed within an hour or so postmortem excludes the autolytic change unless it be conceded that such changes may take place before death, or may be agonal in character. The condition is not associated with vascular disease nor has it been correlated with any particular antemortem conditions. Its existence is of interest purely from the pathological standpoint. A soft brain is not increased in volume or weight as is an edematous brain and the characteristic plasticity of edema is wanting. The softness of the cerebral structures seems to be the only alteration. Normally one can detect by palpation a distinct difference between the frontal and occipital poles and the main mass. This variation in resistance may be destroyed in general encephalomalacia, or the reduction in consistence may be proportional. Southard and Hodskins have reported diffuse axonal reactions and diffuse Marchi degenerations as one of the concomitants. More recently Alzheimer has noted a widespread destruction of the finer glia fibrils in acute infectious processes in the brain. He says "it is noteworthy that with the appearance of the ameboid glia cells, the fibrillar glia may disintegrate to a considerable extent." These changes occur with others which appear in the brain in many acute infective processes and are not specific. Thus in warning against too lax interpretation of the appearance of ameboid glia cells, Alzeheimer states that it must be remembered that severe somatic disease of various types may give rise to an entirely similar picture. This possibility of the destruction by antemortem processes of preformed glia fibrils when considered with our knowledge of the essential rôle of gliosis in the formation of local foci of induration, suggests a possible mechanism of general encephalomalacia.

Chronic Progressive Softening of the Brain.—Wernicke has described a condition of chronic progressive softening of the brain in which through a long course of years progressive focal signs occur without general symptoms. The localization is variable and the condition is probably due to a variety of causes, such as slowly progressive arteriosclerosis, syphilitic endarteritis, thrombosis, etc. Aside from these vascular lesions, however, are cases in which the vessels are reported as normal and yet progressive softening is recorded (Henneberg). Carbon monoxide, phosphorus, and various organic toxins have been advanced as etiological factors. Local foci of primary degenerative encephalitis are also mentioned. The condition may be allied to that giving rise to porencephalic conditions in infants.

Focal Softening of the Brain.—The causes of focal encephalomalacia are numerous. Arteriosclerosis, thrombosis and embolism, and syphilitic endarteritis obliterans are probably the most frequent. Local softenings due to the pressure of tumors, abscesses, and hemorrhages are not uncommon. The mechanics

of this type of softening is probably that of obliteration of capillary fields through pressure which, on account of the viscosity of the brain mass and the resistance of the fibrous septa, is not transmitted equally in all directions. Venous stasis by thrombosis, when complete, gives rise to widespread red softening. Carbon monoxide and phosphorus poisonings are held accountable for focal softenings. Trauma is a not infrequent cause.

At autopsy the cyst varies markedly in appearance. In the gray matter red softenings are frequent, though generally the color varies from pale yellow to reddish brown. This is dependent on first, the amount of reflux hemorrhage and second, the length of time elapsing between the softenings and the autopsy. The yellowish-brown color of the typical plaque jaune is due to the pigment deposited free and in phagocytes in the cyst wall. In the white matter the color is usually bluish-white or gray, occasionally pinkish or yellow, rarely deep red. After a time absorption takes place leaving a cavity filled with clear or grumous fluid. The connective tissue of the pia and vessels is more resistant to ischemia than the brain structures and as a rule the pial covering is intact, while there may be strands of perivascular connective tissue and remains of vessels through the cyst. In a case observed by the writer of a large cyst consequent on syphilitic endarteritis which had destroyed nearly all of one temporal lobe and most of the occipital lobe of one hemisphere, no brain substance remained between the ependymal lining of the dorsal and temporal horns of the ventricle and the pial covering, except several very small masses adherent to the pia along one of the large vessels. The posterior cerebral artery had been the site of extensive disease, but was not completely obliterated and there had apparently been sufficient continuous circulation to maintain the structural integrity of the small masses of brain matter, which were cut off entirely from any connection with the remaining brain substance.

The destruction of the brain substance takes place by means of liquefaction and absorption. Fatty degeneration is the first demonstrable step. Phagocytes of both the endothelial type and of the kind which are usually interpreted as glia cells are present in greater or less abundance, and laden with products of disintegration. Surrounding the area of liquefaction and corresponding to the zone where the blood supply by collaterals must be below normal in amount the nerve elements disappear, while the fibrillar glia is increased in amount, forming, in long-standing cases, a thick mat. There is not in the brain, however, replacement of lost substance at all comparable to the cicatricial replacement of infarcts in other organs of the body. The glia is not able to replace large losses when their occurrence is sudden, and the connective tissue—either because of its small amount or for some unexplained reason—likewise fails to fill the gap. The glia can undoubtedly survive and proliferate in degrees of ischemia in which the nerve elements are lost. One occasionally meets areas where the destruction of parenchymatous structures is complete, but where glial replacement has prevented actual loss of substance. In the case of softening from syphilitic endarteritis described above, the first temporal gyrus of the hemisphere opposite to the cyst of softening had been the seat of such a process and while the gyrus was somewhat shrunken there was no true cyst. Microscopic examination showed that the nerve elements had entirely disappeared and there remained practically a glial cast of the original. This is interpreted as a result of a long-standing partial interference with the blood stream or a gradually progressive and ultimately complete obliteration, resulting in the establishment of sufficient collateral supply to keep the glia structures alive, but not to support the nerve elements.

Acute Red Softening.—Strictly speaking, this condition belongs in the group of the encephalitides and hence may be omitted from full treatment here. As usually accepted it is a result of septic inflammation. *Staphylococcus pyogenes aureus* and the pneumococcus are the most common organisms. (Southard and Keene.) The writer has found a septicemia of *B. pyocyaneus* in one case, though a staphylococcus was also recovered from the meninges. It is characterized by innumerable punctate or larger hemorrhages in the cortex and adjacent white matter and varying degrees of softening from a mere reduction in consistence to a marked diffluent condition.

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Brain, Compression of the.—Cerebral compression is brought about by any condition that causes a contraction of the intracranial space providing that there is no coincident brain atrophy to compensate. The diminished capacity of the cavity of the skull may be due to changes in the bone itself, either general or localized. The latter is sometimes due to overgrowths of bone from the inner table but more frequently due to depressions in the skull of traumatic origin. Any increase in the amount of cerebrospinal fluid such as edema of the brain, hydrocephalus allows less space to be occupied by the brain. Pathological formations may encroach on the intracranial space, including among these not only tumors, aneurysms, etc., but also collections of pus or blood. The pressure within the intracranial cavity is increased by any of the above conditions but whether it is strictly correct to speak of brain tissue as compressible is open to question since it is stated by von Bergmann that its compressibility is less than that of water. There is no doubt, however, that the brain as an organ may be compressed by driving some of the contained cerebrospinal fluid into the spinal cavity or causing its absorption.

The disturbances in the brain resulting from a rapid increase of intracranial pressure, such as would be caused by a large depressed fracture of the skull or the rapid development of a blood clot, probably differ somewhat from those caused by the slowly increasing pressure of a brain tumor. In the former case we must reckon on the more marked disturbances in the vital centers in the medulla, greater disturbance in consciousness, etc., which result from the fact that the cerebral mechanism has no time to adjust itself to the

altered circumstances. A rapidly increasing pressure tends to cause venous stasis which in turn leads to edema and more increase in pressure, the process terminating fatally if continued. With a slowly increasing pressure the brain may be immensely compressed without marked disturbance in consciousness or the development of dangerous circulatory, or respiratory symptoms. That this is due to the slow adjustment of the brain to the altered pressure is shown by the fact that a lumbar puncture done in a brain tumor case may cause the development of these symptoms even though there is, by this procedure, a lowering of the intracranial tension. The sudden change in tension does not permit of time for adjustment.

Light pressure on the brain substance, so long as it does not produce any marked circulatory change in the part pressed upon, is not incompatible with a continued function of that part. More severe pressure causes venous congestion and irritation of the part. A further continuation or increase of the pressure results in softening or degenerative change.

Symptoms.—The symptoms of cerebral compression are divided into the general and local. The character of the former depends somewhat upon the rapidity of increase of the pressure; the character of the latter, upon the part of the brain that is compressed.

Headache is usually an early and constant symptom. It is usually of the bursting or throbbing variety and even the partially unconscious patient indicates his suffering from it. Its location need not necessarily have any relation to the site of the compression.

Vertigo, in some cases, may be a constant symptom; in others the vertigo is present only in attacks.

Disturbance of consciousness is an early and important symptom where the pressure is raised suddenly or rapidy. In such cases dulled sensorium gives place to stupor and, soon after, to deep coma. There are no voluntary movements. The eyes are half-opened, the pupils unequal if the pressure is greater on one side than the other and may show no reaction to light. The breathing is usually stertorous; it may be of the Cheyne-Stokes or Biot type. The skin is hot and moist, the lips blue, and the face congested. The pulse is at first slow and full due to vagus irritation; later on, vagus paralysis is attended by a rapid pulse which, with deepening coma, is a sign of grave import. The conjunctival reflex may be lost. The tendon reflexes may be diminished or lost. Usually there is incontinence of urine and feces. Convulsive twitching may be present. Frequently there is a hemiplegia on the side of the body opposite to the pressure but the deep coma may make it difficult to show this unless by some procedure such as that described by Raimiste in the *Revue Neurologique*, November 30, 1909. Conjugate deviation of the eyeballs is often an aid in the diagnosis. The eyegrounds are usually congested and there may be an edema of the nerve head if the pressure is persistent.

When the increase of pressure occurs more slowly, as it does with brain tumor or abscess, the disturbance of consciousness and the circulatory and respiratory signs are usually much less marked. Tumors the size of a large orange, if located in a so-called silent area, may cause no interference with cerebration. Frequently, however, there is some dulling of thought, the patient is slow to comprehend and respond. General convulsions may occur, attended with loss of consciousness. Vertiginous attacks and even general epileptiform attacks may occur. Attacks of vomiting apparently causeless and unattended with nausea constitute a frequent symptom. The vomiting is likely to be of the "projectile" type. One of the most positive signs is an edema of the optic nerve head, or the so-called choked disc. The disc may be swollen eight to ten diopters and accompanying this there may be retinal hemorrhage. The choking of the disc does not usually cause any disturbance of vision but a continuation of this condition results in secondary atrophy and blindness. A reversal of the normal range of the color field is also a sign of increased intracranial pressure, according to Cushing. Extraocular paralyses, especially external rectus palsy, may occur from the general increase of intracranial pressure. In infancy or in young children there may be changes in the size and shape of the head. The pulse is usually slow and full though in a later stage it may be rapid and weak. Blood pressure is usually increased. Respiration is affected only in the later stages or when some rapid increase of pressure has occurred and is then frequently of the Biot type. The increased intracranial pressure may be directly observed by lumbar puncture.

Diagnosis.—The diagnosis of cases of rapid compression of the brain may be made by the increasing stupor and, later, deep coma with diminished reflexes; the slow pulse, congested face and ocular fundi, and usually some evidence of pressure on a certain part of the brain, such as pupillary inequality, paralyses, Jacksonian epileptic attacks, and the like. The history is of value if it can be obtained. A history of cranial injury which causes no unconsciousness or symptom of concussion, from which the patient recovers and then gradually becomes unconscious, is most suggestive of hemorrhage.

Such cases are to be diagnosed from the unconsciousness in epileptic or hysterical attacks and the comatose stage of certain poisonings, particularly opium or alcohol. The absence of pupiliary inequality, paralysis, or other localizing signs and the presence of other signs of the poisons is sufficient to make the diagnosis. Uremic or diabetic coma sometimes resembles closely that from cerebral compression and a diagnosis in some cases is exceedingly difficult. Other signs of nephritis are necessary to diagnose the former but it should not be forgotten that albumin sometimes occurs in the urine as a result of brain injury; and on the other hand, that nephritis is frequently accompanied by arteriosclerosis and high blood pressure, a condition predisposing to cerebral hemorrhage. Furthermore, uremic poisons may act locally on the brain to produce hemiplegia, epileptic attacks, etc., and then an albuminuric retinitis is not always easily distinguishable from a choked disc. Diabetic coma is more easily distinguished from cerebral compression but it should be remembered that pressure or injury to the floor of the fourth ventricle may cause glycosuria.

The diagnosis of slowly increasing cerebral compression is based upon the presence of headache, vertigo, nausea and vomiting, some disturbance in consciousness, epileptiform attacks, and papilloedema or choked disc. In infants where the cranial cavity can enlarge, these symptoms may all be absent. Usually not all of them are present in any case. Headache is probably the most frequent, although it may be absent. Choked disc is the most reliable symptom but is frequently absent.

The diagnosis of the conditions causing increased intracranial pressure is of the greatest importance from a therapeutic standpoint. There may be some increase in intracranial pressure after trauma to the head even though there is no fracture and no hemorrhage. Weitz has shown that the pressure found by lumbar puncture in such cases may be 200 to 300 millimeters of water and de Schweinitz reports sometimes finding a choked disc in such cases. The pressure is probably produced by a transudation of serum and disappears without treatment; but a continued choked disc may cause the development of a secondary optic atrophy and permanent impairment of vision. Electrical shocks and sunstroke may cause the same phenomena. Cerebral emboli and apoplectic attacks may cause

signs of suddenly increased pressure. Dural hemorrhages are usually traumatic in origin, and result from a tearing of the middle meningeal artery. The characteristic symptoms for all cases of rapid cerebral compression are the same as those described above. Sinus thrombosis, especially the autochthonous thrombosis, may cause marked symptoms of cerebral compression (Camp, Riggs).

Internal hydrocephalus may cause marked compression symptoms, especially the acquired form, coming on after childhood. Such cases are usually due to blocking of the flow of cerebrospinal fluid from the ventricles by a chronic meningitis around the foramen of Magendie, as observed by Bramwell *et al*, or by a tumor which, in its growth, obliterates the cavity of the fourth ventricle as in a case reported by Judson and Camp. A tumor growing in the vicinity of the foramen of Munro may block that opening and cause a unilateral internal hydrocephalus (Camp).

The collection of pus in the meninges in cases of acute meningitis may cause some symptoms of cerebral compression but these are more marked in cases of chronic meningitis, especially in the so-called internal hemorrhagic pachymeningitis. This condition is not infrequently found in chronic alcoholics, and in senile and paretic dements. It is occasionally caused by trauma to the head. The diagnosis of these cases is not usually made antemortem as the symptoms are obscured by the symptoms of the primary affection. Serous meningitis may give rise to pressure symptoms and these cases are frequently mistaken for cases of tumor of the brain. The course of the case and an abscess of definite localizing signs are the chief points of difference.

Cerebritis, encephalitis, and polioencephalitis may cause marked compression symptoms coming on suddenly with fever and other indications of an inflammatory process. They may be of toxic origin.

Abscesses within the brain are not uncommon as a result of trauma, extension of an infectious process from contiguous structures, or a general pyemia. They usually give symptoms of slowly increasing intracranial pressure. Their rate of enlargement is very variable. They tend to become incapsulated and, when surrounded by a strong capsule, may remain latent for years. In such a condition they may produce no symptoms and only be discovered accidentally at the postmortem examination or they may take on renewed activity at any time. The intensity of the compression symptoms varies with the rate of enlargement, but they are of the same general character as those produced by a brain tumor.

Tumor of the brain is one of the commonest causes of slowly increasing cerebral compression. They are of various kinds and the intensity of the pressure symptoms and their character depend not only upon the rate of growth but, to some extent, upon the location of the tumor, being usually more marked when the tumor is beneath the tentorium cerebelli.

Prognosis.—The prognosis in cerebral compression in general depends upon the nature and removability of the cause. In traumatic cerebral hemorrhage the question as to whether there is one or more than one, plays an important part. Where there is only one hemorrhage and the clot can be removed, complete recovery may occur unless the pressure has been so long continued that secondary changes have occurred in the brain cortex. Many of these patients die in spite of operation, possibly from cerebral concussion and the added shock of operation. Accurate and early diagnosis of the cause is a first requisite for efficient treatment; without that only palliative measures can be adopted.

Treatment.—The treatment of cerebral compression is the treatment of the cause of the compression if a permanent cure is to be looked for. In the main, such treatment is surgical although gummata may be influenced by potassium iodide and mercury and the treatment of chlorosis, myexdema, etc., may result in a lessening of the symptoms if due to these causes.

A decompression of the brain by removal of a part of the skull may be necessary if the cause of the compression is not definitely known or if it appears to be irremovable. In the case of an irremovable brain tumor it may make the patient more comfortable, prolong life, and preserve the eyesight. The indications for decompression may, therefore, be summed up as: intolerable headache or vomiting; marked circulatory or respiratory symptoms due to pressure; or choked disc which is persistent and which, if it continued, would lead to optic atrophy and blindness. Such decompression operations may be done at almost any point of the skull but the temporal region is favored by many as being easy of access and the temporal muscle affords some protection to the uncovered brain. The actual amount of protection, however, is very slight since almost invariably in such cases the development of a cerebral hernia causes atrophy of the muscle. The headache and vomiting are usually promptly relieved by decompression; the choked disc also subsides, as a rule, and the patient is much more comfortable.

Lumbar puncture has also been advocated as a method of reducing intracranial pressure but it is not without danger in such cases. Almost all the deaths that have occurred from lumbar puncture have been in cases of brain tumor and this is attributed either to a too sudden change in intracranial pressure or, what is more likely, to a disturbance of the pressure equilibrium between the cranial and spinal cavities, the result being that the medulla is forced down into the foramen magnum like a cork into a bottle and the vital centers in the medulla are thereby paralyzed.

Ventricle puncture is probably a safer procedure than lumbar puncture in these cases. von Bergmann suggests boring a hole in the skull with a Doyen burr a little above and internal to the tuberosity on the frontal bone and passing a hollow needle from before backward and a little downward until fluid flows. Keen chooses a point in the parietal region for the same procedure. Unfortunately, the effects of either lumbar puncture or ventricular puncture are but temporary and there is always danger of infection or setting up a traumatic encephalitis. Various procedures have been attempted for the permanent drainage of the ventricles but they have all been either unsuccessful in their object or followed by fatal results. A stiff drainage tube causes too much traumatism to the brain as it pulsates, a soft tube does not drain well.

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Brain, Concussion of the.—Cerebral concussion or jarring of the contents of the cranial cavity may be produced either by direct impact on the cranium or by a jar transmitted through bones that are contiguous to the skull, such as the spine or the bones of the face. The knockout blow on the lower jaw is a good illustration of the latter.

The degree of concussion depends upon the force

of the blow, the area of impact, and the direction of the impact. A series of light blows may produce the same amount of concussion as one more severe blow, as shown by the experiments of Koch and Filehne on animals. Owing to the ovoid shape of the skull the direction of the blow exercises a very considerable influence on the degree of displacement and compression of the brain that will result. The investigations of Kocher and Ferrari would show that the effect is greater when the impact is on the lesser diameters although, owing to the semifluid consistency of the brain, the pressure is transmitted in all directions.

There is a considerable difference of opinion as to what actually takes place in the brain to cause the symptoms of cerebral concussion. On the one hand it must be admitted that the clinical symptoms are often so transient that one cannot conceive of an organic change as their basis and, in some cases, even so severe as to cause death, no demonstrable pathological change is found at necropsy. For such cases various explanations are offered. Shock, with transitory cerebral anemia, is a frequent explanation, borne out to some extent by the clinical symptoms and by the rapid and apparently complete recovery seen in many cases. Molecular change in the nerve cell, causing a transient inhibition of function, is another explanation which would account for the fact that degenerative changes occasionally follow. Another explanation is that, as the white matter has a greater consistency than the gray, it would be more displaced as the result of an impact and a slight cleavage, sufficient to inhibit function, would take place between the white and gray matter.

By many authors concussion of the brain is regarded as synonymous with contusion of the brain. In the latter there is more or less laceration of brain substance, and miliary hemorrhages brought about by the tearing of capillary blood-vessels. Such a condition is rarely followed by a complete *restitutio ad integrum* and the symptoms will depend, to a considerable extent, upon the part of the brain most injured.

Symptoms.—The most striking symptom of concussion of the brain is a disturbance of consciousness. This may be light and only momentary in duration or it may be a total loss of consciousness which resists all efforts at restoration and persists for days and even weeks. The author examined one case in which there was practically complete loss of consciousness for four weeks following a severe blow on the head. The patient then gradually recovered consciousness with no paralysis nor any other permanent symptoms. In light cases the patient may not fall but becomes confused, his face is pale, the skin cold and damp and he feels weak and dizzy. He becomes nauseated and may vomit but soon reacts with, usually, a severe headache. The pulse is usually rapid and weak. In more severe cases there is muscular relaxation, though rarely to the extent of loss of the tendon reflexes, and the patient reacts only to strong stimuli and then only momentarily. The skin is cold, especially in the extremities, the pulse very weak and rapid, and the skin covered with perspiration. Sometimes there is incontinence of urine and feces. The pupils are usually equal, they may be dilated but contract if a bright light is thrown in them. This stage is usually followed by a stage of reaction in which the patient is nauseated and vomits, shows marked dizziness on change of position and is very irritable, sometimes almost maniacal. The pulse becomes normal and the temperature a little higher than normal. There is usually a severe headache which may last for weeks or months. A transitory blindness may result from cerebral concussion. Wilbrand and Sanger have collected seven such cases from the literature and cases have also been reported by Hirsch and by A. R. Allen. In the case reported by Allen, there was also a unilateral Babinski reflex which disappeared inside of twenty-four hours.

If laceration of brain substance has occurred, there may be, in addition to the above symptoms, evidence of a localized cerebral lesion, such as twitching and Jacksonian epileptic attacks or even generalized convulsions, paralyses, anesthesia, aphasias, and disturbances in the special senses. Also in such cases signs of increased intracranial pressure are soon evident if the lesions are severe.

Sequelæ.—The result of light concussion is usually recovery with only a temporary discomfort although headache may persist for some time. This, as Weitz has shown, is probably due to an increased intracranial pressure since the cerebrospinal fluid is shown, by lumbar puncture, to be under increased pressure in such cases.

There is frequently a complete amnesia for the accident causing the concussion and sometimes for occurrences which preceded the accident. This so-called retrograde amnesia is illustrated by a patient of mine who had visited another city on business. In the evening he was struck by an automobile and sustained a severe cerebral concussion. He recovered from this but with an entire loss of memory of the day's events. Although he had transacted business all that day he had no recollection of anything after leaving home in the morning.

A not uncommon sequel to cerebral concussion is the development of a traumatic neurosis. While, in these cases, the symptoms are probably due to the psychic shock rather than to the brain injury, the differentiation is sometimes exceedingly difficult.

An extensive cerebral softening has been described as a result of cerebral concussion; in such cases, however, there are probably other factors also at work. The traumatic late apoplexy (*spät-apoplexie*) is also to be considered as among the sequelæ. Opinions differ as to whether the rupture of the blood-vessel is due to a degeneration of the vessel wall or to a degeneration of the brain tissue about the blood-vessel thus depriving it of support.

The development of epilepsy after concussion of the brain may probably be ascribed to laceration of brain substance which is followed by a localized gliosis. In one case that I have seen a cerebral concussion was followed by the development of a localized serous meningitis. The chief symptom was epileptic attacks of the Jacksonian type and the patient was relieved by trephining over the affected area.

Traumatic encephalitis is a not infrequent occurrence as a sequel of cerebral concussion and this in turn may lead to the development of brain abscess. Such abscesses are not caused by any direct infection of the brain but probably develop because a *locus minoris resistentiæ* is formed by the concussion. These abscesses are sometimes situated deep within the brain, as I have seen in two cases.

Paresis has been described as a sequel of cerebral concussion. Careful study, however, shows that a positive Wassermann reaction can be obtained in such cases and the trauma, if it stands in any causal relation to the disease, simply excites to activity a latent process.

Barany has called attention to the presence of marked cerebellar symptoms following cerebral concussion. I have observed such a case with necropsy but no demonstrable organic changes were found in the central nervous system.

A number of cases are on record in which a cerebral concussion has been the apparent exciting cause of the growth of a brain tumor.

The prognosis of cerebral concussion should always be guarded, especially if there are any signs of cerebral laceration, on account of the numerous grave sequelæ that may develop.

Treatment.—The treatment of the initial symptoms of cerebral concussion is the treatment of shock—a recumbent posture, warmth applied by hot water bottles and warm covering. Stimulants may be necessary such as: inhalations of aromatic spirit of ammonia, the faradic brush to various parts of the body and the hypodermic administration of strychnine or ether and camphorated oil. Artificial respiration may be necessary. Care should be taken not to overstimulate for fear of causing a violent reaction. During the reaction stage an ice-bag to the head may give some relief and the patient should be kept quiet and isolated. Morphine is advised by some but condemned by others on the grounds that it increases venous congestion. It is probably better not to use it. For the insomnia we may use veronal or chloretone.

The patient should keep on a light diet and avoid overexertion or excitement for some time after such a trauma. Lumbar puncture is sometimes of value in relieving the persistent headache and dizziness.

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Brain, Diagnosis of Local Lesions of the. History.—Although it was known in the first century that each hemisphere of the brain is in functional relation with the opposite half of the body, the facts upon which the prevailing theory of the localization of different functions in separate parts is based were not discovered until 1822. At that time, Thomas Hood in England, and Bouillaud in France, noticed that disturbances of speech were caused by disease in the frontal lobes of the brain. M. Dax (1836) was the first to limit the area governing speech to the left frontal lobe, and Broca (1861) located it more exactly in the left third frontal convolution. The discussion of aphasia in the Academy of Medicine in Paris in 1864 awakened general interest and led to further investigation. Until that time scientific men, rejecting the unwarrantable conclusions of Gall and the phrenologists, had believed the teachings of Flourens, that the brain acts as a whole, its various parts not possessing various powers. The pathological evidence against this position collected by Broca, and strengthened during 1864–67 by facts observed by Hughlings Jackson and Meynert, received confirmation in 1870 from a new series of physiological experiments made by Fritsch and Hitzig in Berlin. These investigators found that in animals the anterior portion of the convexity of the brain is motor; that its irritation by electricity causes coordinated motions in the limbs of the opposite side, and that its destruction causes paralysis. Ferrier (1873–76), Nothnagel (1877), Munk (1881), and Luciani (1884) confirmed these results, and showed further that the posterior portion of the convexity is sensory, its destruction being attended by impairment of the powers of perception through the various senses. Goltz, though opposing a strict limitation of functions to definite regions, admitted that the results of destruction of various parts are different, and he noticed that extensive injury to the anterior portion changes the character of an animal from kind to vicious, while injury to the posterior portion has the opposite effect. The conclusions of physiologists differ regarding the results of experiments, but do not overthrow the theory of localization as applied to man; for a mass of pathological evidence has been collected which will bear but one interpretation. Charcot and his pupils in France, Nothnagel, Exner, and Wernicke in Germany, H. Jackson and Ferrier in England, and others, have gathered, classified, and analyzed a very large number of cases of brain disease of limited extent, which were accompanied by definite symptoms, and have established a causal relation between lesions of certain portions of the brain and disturbances of certain functions, both motor and sensory. It has also been discovered that deficient development of an organ is accompanied by deficient development of that part of the brain which is in functional relation with that organ, and *vice versa* (von Gudden).

Further, the researches of Flechsig (1877–99) have proven that an anatomical connection exists between certain organs and certain parts of the brain by means of tracts, which can be distinguished from one another by peculiarities in the time and process of their development; and that each functional area of the brain has its own period of development during the early months of life. To these same tracts are limited the secondary changes which ensue when the active organ at one extremity of the tract is destroyed. Furthermore Campbell (1900) has shown that the cortical structure of the brain differs in different regions, which offers a probability that their functions differ.

All these various kinds of evidence combine to establish the conclusion that definite parts of the brain possess distinct functions, and although there remain numerous functions whose location is unknown and many parts of the brain whose function is undetermined, a sufficient number of facts is available to warrant, in many cases of cerebral disease, a localization of the lesion.

General Considerations.—Since the different parts of the brain preside over different functions, the symptoms present in any lesion will depend as much upon its situation as upon its nature. Certain general symptoms, such as headache, vertigo, convulsions, coma, or optic neuritis, occur in many forms of disease, and being indications of disturbances of nutrition, or of increased intracranial pressure, do not indicate the position of the disease. Other symptoms, however, such as disturbances of motion, of sensation, of sensory perception, of memory, or of speech, are known as local symptoms, since each is present only when a certain part of the brain is involved. It is from these that the localization of a lesion can be determined. Local symptoms must, however, be interpreted with caution, and the direct effect of the lesion must be distinguished from its indirect effect. For example, immediately after a cerebral hemorrhage, attended with headache, vertigo, or coma, and possibly general convulsions and vomiting, the local symptoms of hemiplegia, hemianesthesia, and aphasia may be present, and may lead to the suspicion of a very extensive lesion. After a few days, however, there may remain only a partial hemiplegia, all other symptoms having subsided. In such a case the hemiplegia is the only direct local symptom; the indirect local symptoms—aphasia and hemianesthesia—being incidental to the pressure on, or to disturbance of, circulation in parts adjacent to the actual seat of disease. It is only when a lesion is single, its effects stationary and of some duration, that a diagnosis of its position is to be made.

In diagnosticating the position of a lesion it is necessary to distinguish disease in the cortex from disease within the hemisphere. The functions of these parts are different. The gray cortex receives and initiates impulses. The white matter within the hemisphere transmits the impulses. The impulses sent along white tracts to the cortex become conscious perceptions only when they reach their destination in the gray matter. The impulses passing along the white tracts from the cortex have been started in the gray matter as conscious volitions by effort. Thus

sensation or motion may be suspended either by disease in the cortex or by disease in the tracts within the hemisphere. The cortex has another function. A sensation once perceived, or a motion once acquired, leaves behind it a trace, whose nature is unknown, which shows itself in a disposition in the cells of the cortex to react more promptly to a similar impulse than to a dissimilar one. This is the physical basis of memory. Since similar impulses always enter by the same sensory organ, and since each organ is connected with its own region of the cortex, it follows that the various memories are distributed in various regions. But these memories are often associated in consciousness, and this association is secured by means of white fibers which pass between and connect the various regions. It becomes evident, therefore, that diseases of memory may afford an important clue to the location of a lesion; and that the distinction between a disease of the gray cortex involving a loss of a certain kind of memory, and one of the white tracts within the hemisphere interfering with the proper association of ideas must not be overlooked. No part of the gray matter can act vicariously for another part. Each tract conveys its own impulses.

Diagnosis.—I. *Cortex Cerebri.*—1. Lesions involving the frontal lobes upon the base may destroy the olfactory bulb or tract and produce anemia on the side of the lesion. Lesions in the other convolutions of the frontal lobes, excepting those in the posterior part of the third convolution of the left side, present no distinctive local symptoms. Some disturbance of mental action, manifested by an inability to concentrate the attention, to think connectedly, and to control the emotions, or even by a condition of imbecility, may be caused by disease in this region; and lesions in the frontal lobes often cause a loss of control over the sphincters.

These convolutions are often defective in idiots, and their comparative development in animals determines the mental power of the individual. But disease in this region in man does not cause a loss of any particular mental faculty, and for the higher powers of mind no location can be determined. Normal mental action implies the integrity of the entire brain. When general symptoms of cerebral disease are present, but no local symptoms can be found, the possibility of disease in the frontal convolutions is to be considered, and the occurrence of the mental disturbance mentioned affords a presumption in favor of this location.

Lesions in the posterior part of the third frontal convolution on the left side in right-handed, and on the right side in left-handed persons give rise to ataxic or motor aphasia (Fig. 1008). In this area are located the memories of the combination of motor acts necessary to the pronunciation of words, memories which have been acquired by practice. If these memories are blotted out, the ability to initiate the impulse required to produce a given sound is lost, and speechlessness results. When this convolution alone is affected the patient can understand what is said to him, but cannot talk (see *Speech, Disorders of: Aphasia*).

2. Lesions of the anterior central convolution and of the paracentral lobule produce disturbances of motion (Fig. 1008). The motor tracts which connect these convolutions of each hemisphere with the body decussate partially in the medulla, and the degree of the decussation differs in different individuals. In the large majority of persons the tracts which cross to the opposite side are so much larger than those which go to the same side that the symptoms of cerebral disease are noticed only on the side of the body opposite to the side of the lesion. In all cases, however, except in those in which the decussation is complete (one in sixty), the side which is apparently normal is slightly affected. The disturbance of motion may be in the form of spasms and convulsions, or in the form of paralysis. Lesions irritating the motor region give rise to the former; those which destroy the cortex to the latter. The lower third of the anterior central convolution is in functional relation with the muscles of the face and tongue (Fig. 1008). The middle third of the anterior central convolution governs the arm (Fig. 1008), the motions of the shoulder, elbow, and hand lying from before backward and from above downward in the order named. The upper portion of the anterior convolution and the paracentral lobule contain the motor centers for the body and leg, the motions of the hip, knee, and foot lying from before backward and from above downward in the order named. The area related to the movement of the

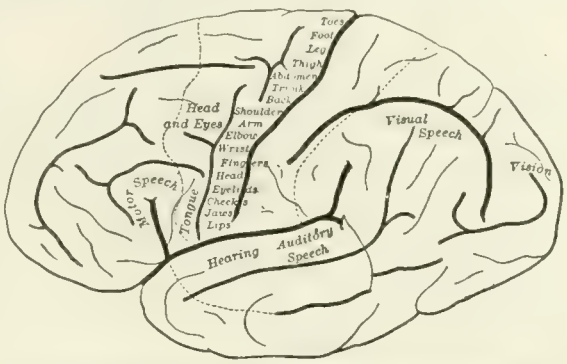

Fig. 1008.—Diagram of the Fissures and Convolutions of the Convexity of the Left Hemisphere of the Brain, with the Areas Presiding over Various Functions. The speech areas are shown on this hemisphere. The motor area is more extensive on the left than on the right hemisphere.

eyes is located just in front of the area for the arm in the posterior part of the middle or second frontal convolution. As these areas for each part are distinct, cortical lesions of limited extent may affect one alone, or two adjacent areas; but it is only lesions of very great extent which can destroy them all. Monospasms, or monoplegia, are, therefore, prominent symptoms in disease of the motor region. An irritation beginning in one area may extend to adjacent areas, in which case a convulsion may commence in one part and then involve other parts. The relative position of the areas, then, determines the order of progress of the convulsion, face, arm, and leg being successively affected, or *vice versa;* and face and leg never being involved together without affection of the arm. When the entire side is involved the convulsion may become general. The seat of the initial irritation may, therefore, be indicated by the order in which the spasms extend. After such a spasm there remains a paresis in the muscles affected, those last and least involved recovering first (see *Epilepsy*). If the irritating lesion becomes a destroying lesion the monospasm is succeeded by monoplegia, and from the part of the body affected the area in the motor region which is destroyed can be determined. In cortical disease it is seldom that the lesion involves a single area without encroaching upon adjacent areas; hence, associated monoplegiæ of face and arm, or arm and leg, are more frequently met with than paralysis of one part alone. But even in these cases the disturbance of motion usually begins or is more marked in one part, rather than in both equally, and the order of extent of paralysis may indicate the direction in which the disease is progressing, and the place from which it started.

In paralysis from cortical lesion there is a loss or marked impairment of the muscular sense, and there may be some disturbance of general sensation. A loss of motor memories, *e.g.* the motions involved in writing, playing an instrument, using a tool, occurs in

cortical disease, and may indicate that the seat of the lesion is in the area of the arm. The limits of the region receiving impulses which awaken the perception of touch, temperature, and pain are not fully determined. It is thought, however, that the motor and sensory regions coincide, while it is probable that the sensory region extends beyond the motor and includes the posterior central convolution and parietal lobules which lie posterior to the motor area. Ferrier, however, teaches that the gyrus hippocampus is the region in which these sensations are received. Lesions affecting the posterior central convolution give rise to sensory symptoms, the sensory areas lying in the same order as the motor areas, face, arm, and leg in the lower, middle, and upper thirds respectively. Lesions in the motor area anterior to the fissure of Rolando usually produce paralysis without anesthesia. Lesions in the parietal lobules may produce anesthesia but do not cause paralysis.

Each sensory area is in functional relation with the opposite limb to a much greater degree than with the limb of the same side. Monoanesthesia may therefore occur from cortical lesion. The loss of sensation is rarely total, as it is probable that the decussation of sensory impulses is rarely complete. The degree of impairment of sensation is to be ascertained only by comparison of the affected limb with the other three. If the sensory area is not destroyed but is only irritated, subjective sensations in the limb whose area is affected occur, and such monoparesthesiæ are valuable indications of cortical lesion, when disease in other parts is excluded.

Monospasm and monoplegia, monoparesthesia, or monoanesthesia, are therefore the chief symptoms of cortical disease in the sensorimotor area. The two former indicate an affection lying anterior to the fissure of Rolando: the two latter lesions posterior to that fissure. No local symptoms of disease in the parietal lobules are known, the disturbances of speech or of sight which occur occasionally when the supramarginal gyrus is involved being due to a coincident lesion of the tracts passing beneath it.

3. Lesions of the three occipital convolutions and of the cuneus produce disturbances of vision (Fig. 1009, D). Each occipital lobe is in anatomical connection with the like-named half of each retina, and hence a lesion of one occipital lobe produces an affection of vision in the opposite half of both visual fields. The visual tract terminates in the cuneus, the upper part of which is related to the lower half of the retina and the lower part to the upper half. The fibers to the cuneus pass so near to the cortex of the convexity of the occipital lobe that lesions in the lobe are likely to cause the same symptoms as lesions of the cuneus. Irritation of the cortex of this region may cause hallucinations of vision, and if the irritation is in one lobe the subjective sights will appear upon the opposite side of the median line, and will move with the eyes of the patient. Destruction of the cortex will produce bilateral homonymous hemianopsia, *i.e.* blindness in the opposite half of both eyes, and may also cause a loss of visual memories; the patient will fail to recognize familiar objects, and cannot recall scenes and faces formerly known. If the lesion is in the left occipital lobe near to its junction with the inferior parietal lobule (see Fig. 1008), written and printed language also may no longer be recognized, and the patient, therefore, may lose the power of reading while speech remains. This condition is known as alexia. If the capacity to recognize objects by touch is lost the condition is termed asteriognosis. This is often due to a lesion involving the tracts under the junction of the occipital and parietal convolutions, or in the parietal lobe. It indicates a destruction of association fibers by means of which the memories are grouped. The relation of the angular gyrus, which lies anterior to the occipital lobe, to vision is undetermined. While it was formerly supposed to be the center of the visual area by Ferrier, this view has been opposed by German authorities, who hold that the disturbances of vision which have occurred occasionally when it was diseased have been due to a lesion of the visual tract which lies beneath it and which passes to the occipital lobe (see *Hemianopsia*).

4. Lesions of the first and second temporal convolutions produce disturbances of hearing, each lobe being related to both ears. Irritation of these convolutions may cause hallucinations of hearing, and destruction of them may cause deafness. If the lesion is upon the left side and involves the first convolution, the symptom produced is word-deafness,

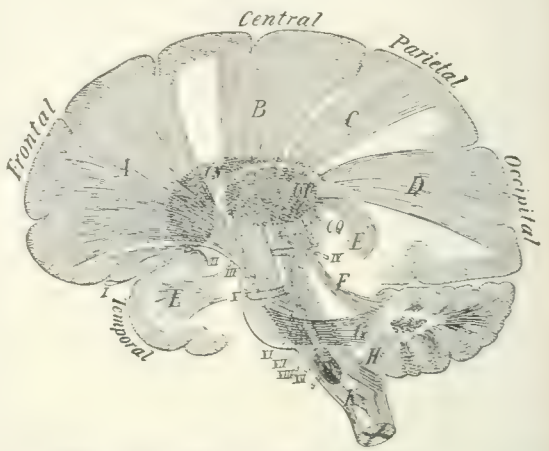

Fig. 1009.—The Projection Tracts Joining the Cortex with Lower Nerve Centers. Sagittal section showing the arrangement of tracts in the internal capsule. A, Tract from the frontal lobe to the pons, thence to the cerebellar hemisphere of the opposite side; B, motor tract from the central convolutions to the facial nucleus in the pons and to the spinal cord; its decussation at K; C, sensory tract from posterior columns of the cord, through the posterior part of the medulla, pons, crus, and capsule to the parietal lobe; D, visual tract from the optic thalamus (O.T.) to the occipital lobe; E, auditory tract from the internal geniculate body (to which a tract passes from the VIII. nerve nucleus) to the temporal lobe; F, superior cerebellar peduncle; G, middle cerebellar peduncle; H, inferior cerebellar peduncle; CN, caudate nucleus; C.Q., corpora quadrigemina; Vt., fourth ventricle. The numerals refer to the cranial nerves.

or loss of memory of the sound of words, with consequent inability to recognize the meaning of spoken language or to recall the words necessary to speech. This is also known as sensory or amnesic aphasia or word-deafness. It can be distinguished from motor or ataxic aphasia by the inability of the patient to understand what is said to him (see *Speech, Disorders of: Aphasia*).

5. Lesions at the apex of the temporo-sphenoidal lobe may produce disturbances of taste and smell. If this region is irritated—as by the growth of a tumor of the pituitary gland or elsewhere—hallucinations of taste or smell are produced. These sometimes occur as an aura of epileptic attacks and then indicate the beginning of organic disease.

6. Lesions of the island of Reil have caused disturbance of motion in the face and arm of the opposite side, and also have caused aphasia when the left island was involved. It is not certain, however, to what extent these symptoms were dependent upon the affection of adjacent convolutions, of tracts beneath the island, or of the basal ganglia (Figs. 1010 and 1011). The associating tract which joins the sensory with the motor speech centers lies just under the convolutions of the island of Reil and destruction of this tract causes paraphasia. Lesions of the island of Reil would be especially liable to affect the circula-

tion in the motor area, since the branches of the middle cerebral arteries pass over it. While, therefore, it can be stated that hemiplegia and aphasia may be produced by lesions here, it is probable that they

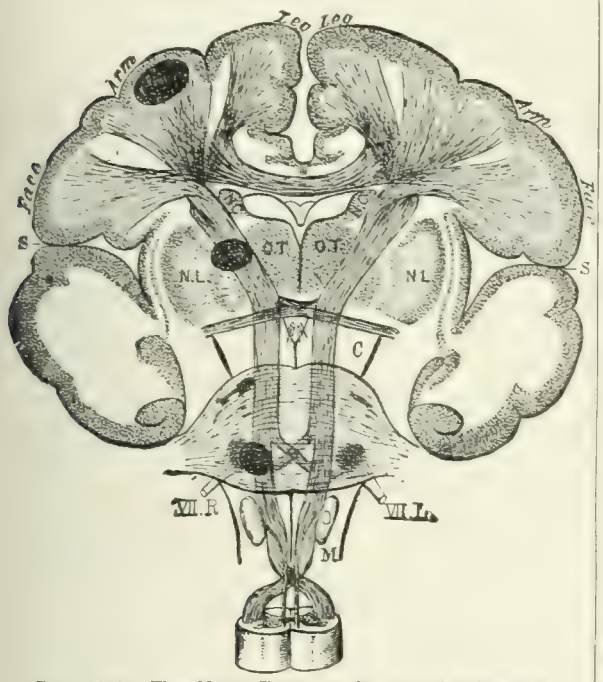

FIG. 1010.—The Motor Tract. S, Fissure of Sylvius; N.L., lenticular nucleus; O.T., optic thalamus; N.C., caudate nucleus; C, crus; P, pons; M, medulla; O, olivary body. The tracts for face, arm, and leg gather in the capsule and pass together to the lower pons, where the face fibers cross to the opposite VII. nerve nucleus, while the others pass on to the lower medulla where they partially decussate, to enter the lateral columns of the cord; the non-decussating fibers pass to the anterior median columns. The effect of a lesion situated at three points in the tract is shown on the left side of the figure.

would be indirect and not direct local symptoms. The function of the island of Reil is unknown.

The facts which have been stated regarding cortical lesions are based upon autopsies and are independent of any physiological considerations regarding the functions of the various parts, although they agree with the results of experiment on animals. It is evident that disease which affects an extensive region of the cortex may produce a number of symptoms arising from the implication of several areas at the same time. Such widespread disease is usually attended by general symptoms, marked mental disturbance, loss of memory, and lack of self-control, as well as by the local symptoms.

II. CEREBRAL TRACTS.—1. The white matter of the brain consists of fibers of two varieties: association fibers which join the different convolutions and functional regions with one another, and projection fibers which join the different convolutions with the basal ganglia and with the gray matter of the pons, medulla oblongata, and spinal cord. These fibers are so interlaced in the centrum ovale that neither can be injured without affecting the other. An interference with the passage of impulses through association fibers produces symptoms of a mental character. An example of this has been cited in describing lesions of the island of Reil, viz., paraphasia. The patient suffering from this disease can recall the desired words, and is able to initiate the motions necessary to speech; but the associating tract between the memory of a definite word and the memory of its motion being broken, he does not speak the desired word but replaces it by another. Thus, in a case known to the writer, whenever the patient spoke she said, "Ah, dear me, I don't know," much to her own annoyance, as she understood what was said to her and knew what she ought to say in reply. The forms of paraphasia, or transcortical aphasia, are numerous, but are all to be referred to lesion of association fibers. It is very probable that many defects of memory, and much of the apparent dulness of mind in brain diseases, are to be ascribed to a failure of function in these fibers by which ideas are associated. Nothing more definite can be stated regarding their injury, and the mental symptoms, aside from paraphasia, do not indicate the location of the disease.

2. Lesions of projection fibers produce well-marked local symptoms. It is by means of these fibers that all parts of the body are joined to connecting parts of the brain, so that in imagination a map of the body can be projected upon the cortex of the brain. An interference with any separate bundle of fibers will therefore produce symptoms in the organ with which it is joined, and therefore will cause effects somewhat similar to those produced by a lesion of the corresponding part of the cortex. It is necessary to consider the lesions of the various tracts, as they produce different symptoms. The projection fibers passing inward and downward from the extensive cortical surface of each hemisphere converge, and are finally collected into a compact tract which lies between the basal ganglia and is known as the internal capsule. Many fibers pass into the basal ganglia, but their function is only conjectured, and the effect of their destruction is unknown. Others pass between the ganglia, through the capsule, and issuing from its basal portion enter the crus cerebri, and traversing it go down to the pons, medulla, and cord.

Since the fibers passing through the capsule are gathered from distant and widely separated regions of the cortex, a small focus of disease in the capsule may produce as serious and widespread symptoms as disease of great extent in the cortex. Extensive disease in the cortex, or in the centrum ovale, produces considerable mental impairment, but this is not true of capsular disease. Hence in any case in which the symptoms are extensive, but the mind

FIG. 1011.—The Association Fibers in the Centrum Ovale. A, Between adjacent convolutions; B, between frontal and occipital lobes; C, between frontal and temporal lobes, the cingulum; D, between temporal and frontal lobes—lesion of this tract causes paraphasia; E, between occipital and temporal lobes—lesion of this tract causes word-blindness; C.N., caudate nucleus; O.T., optic thalamus.

unimpaired, the probability is in favor of a small lesion in the brain tracts rather than of a large lesion in the cortex. The brain tracts in the capsule may be injured either directly, by lesions in their course, or indirectly, by lesions in the basal ganglia in whose vicinity they pass. In both cases the initial symp-

toms will be the same if the disease begins suddenly; but in the latter case recovery may follow, while in the former the symptoms may increase in number, owing to secondary degenerations following a lesion of a tract. If the disease is a slowly progressive one (*e.g.* tumor), general symptoms may precede local symptoms, and indirect local symptoms will be succeeded by direct local symptoms.

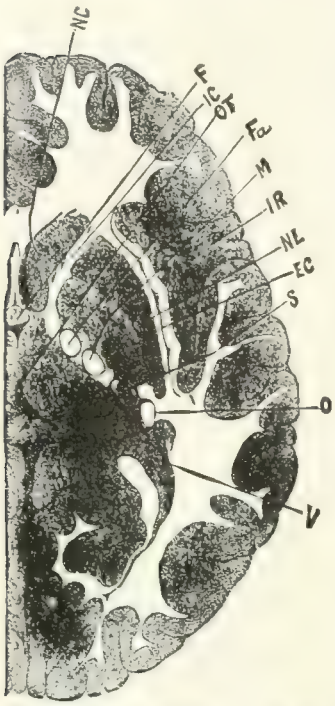

Fig. 1012. Horizontal Section through the Brain. (After Strumpell.) *NC*, Nucleus caudatus; *F*, fornix; *IC*, anterior half of internal capsule; *OT*, optic thalamus *Fa*, facial tract; *M*, motor tract; *S*, sensory tract; *O*, visual tract, in posterior half of internal capsule; *IR*, island of Reil; *NL*, nucleus lenticularis; *EC*, external capsule; *V*, lateral ventricle, posterior cornu.

The internal capsule is divided into two halves, an anterior and a posterior division, by the projection of the apex of the lenticular nucleus, which lies on its outer side. Through the anterior division pass the projection fibers from the frontal lobes (Fig. 1012, IC.), and the fibers which join the anterior parts of the cortex with the basal ganglia. Nothing is known as to the exact function of either of these bundles of fibers, and no symptoms of their injury can be stated. Extensive lesions may occur in the white matter of the frontal lobes, affecting both association and projection tracts without producing any symptoms, although in many such cases the symptoms present in cortical lesions of the frontal lobes do occur. Through the posterior division of the internal capsule pass several important tracts. These are (1) the motor tract from the lower third of the central convolutions, which curves over the lenticular nucleus and passes down in the anterior part of the posterior division of the capsule, enters the second quarter of the crus, thence passes into the median part of the ventral half of the pons, and turning downward ends in the facial and hypoglossal nuclei (Fig. 1012, *Fa*); (2) the motor tract from the other thirds of the central region (Fig. 1012, M), which is known as the pyramidal tract, since its fibers, after passing through the third quarter of the crus and the ventral portion of the pons, make up the pyramid of the medulla; (3) the tract conveying general sensations from the entire body (Fig. 1012, S), which lies just behind the pyramidal tract, and having come from the tegmentum of the crus, and passed through the posterior third of the capsule, radiates toward the parietal convolutions; (4) the visual tract, whose fibers, issuing from the pulvinar of the thalamus, pass upward and turn backward in the capsule on their way to the occipital lobe (Fig. 1012, O); (5) the auditory tract, which passes through the lower posterior segment of the capsule on its way from the auditory nucleus to the temporal lobe (Fig. 1009, E). Lesions of the internal capsule which affect one or more of these tracts cause distinct local symptoms. Lesions in the motor tract produce paralysis, whose distribution will depend upon the extent to which the tract is involved. Usually the entire tract is affected and hemiplegia results; but occasionally the facial and hypoglossal muscles are only slightly affected. In all cases the upper branch of either facial nerve escapes, since its cortical centers are bilateral. In lesions of the pyramidal tract the arm and leg of the opposite side are always paralyzed together. Lesions lying in the sensory tract cause hemianesthesia, which is rarely absolute, but usually in the form of great impairment of sensation on the opposite side from the lesion. Lesions lying still farther back may affect the visual tract and cause blindness in the opposite half of both eyes. Lesions in the lower part of the capsule may produce loss of hearing in the opposite ear. Whether taste and smell are ever affected by capsule lesions is undetermined.

It is evident that an extensive lesion in the capsule may involve two or more of these tracts; and hemiplegia, with hemianesthesia and hemianopsia, could not be produced by a single lesion lying in any other part. The initial effects of a hemorrhage or thrombosis, which involves the internal capsule, may be extensive, as several tracts may be affected. If but one, however, is really destroyed, the affection of the others will be temporary, and the symptoms will decrease in extent and severity until they are limited to the affected tract. It is only after the temporary effects have subsided that the disease can be located accurately. On the other hand, a slowly progressing lesion, tumor, or abscess may involve one tract after another in succession, and the progress of the case will determine the localization of the lesion.

3. Aphasia may be due to a lesion in the tract which joins the third frontal convolution with the facial and hypoglossal nuclei in the pons. Two courses have been described as taken by this tract. One corresponds to the course of the fibers from the face area of the motor region through the internal capsule, already detailed. The other is from the frontal region, backward, crossing at right angles the motor tract, and going along the upper border of the lenticular nucleus, in the external capsule, to its posterior limit, where it curves over the nucleus and enters the internal capsule near the sensory tract, then crosses this tract to the second quarter of the crus, and so reaches the pons. Lesions in the course of either of these tracts have produced aphasia when in the left hemisphere. Such an aphasia resembles ataxic or motor aphasia, and is not to be distinguished from it. It is more liable to be associated with agraphia than when the lesion is in the frontal convolution, as association fibers are likely to be destroyed when the lesion is in the centrum ovale.

4. Lesions of the cortex and of the tracts as they are collected in the capsule having been considered, it is evident that lesions of the centrum ovale, through which the tracts pass on their way from one to the other, will produce similar effects to those in either part, according as it lies nearer one or the other. The association fibers which pass through the centrum ovale are shown in Fig. 1011. Any interference with them will produce defects in the association of concepts and ideas, and hence be shown by mental defects, especially defects of memory. Lesions of the centrum ovale have no distinctive symptoms by which they can be differentiated from lesions in the cortex or capsule, unless the affection of association fibers as well as of projection fibers adds distinct mental symptoms. If the lesion is so situated as not to affect any of the projection tracts it will not produce any local symptoms.

III. Lesions of the Basal Ganglia are very frequent and give rise to many symptoms. These symptoms are, however, to be ascribed to a coincident affection of the tracts just mentioned, which pass

through the internal capsule between the ganglia (Figs. 1012 and 1013), and hence the local symptoms of lesions in the lenticular or caudate nucleus and optic thalamus are those of lesions of the internal capsule opposite those bodies, viz., in its posterior division. If the symptoms are permanent, the capsule is probably injured. If the symptoms pass away, the capsule was incidentally affected. And the effects of the lesion may entirely subside while the lesion remains, if it is limited to either of these ganglia. It is therefore evident that we cannot locate a lesion in the ganglia from any direct local symptoms; for, as we are ignorant of the function of the ganglia, we do not know what is the effect of their destruction. Hemichorea and hemiathetosis occasionally remain after lesions of the thalamus and are to be regarded as symptoms of irritation. The optic thalamus is a sensory ganglion and acts as a center for the reception of impulses which give rise to many reflex or automatic acts, *e.g.* the variations of facial expression. Permanent lesions in it, which cause irritation, may give rise to spontaneous pains in the opposite side of the body, or to an excessive appreciation of ordinary or slightly painful stimuli, and to minor degrees of anesthesia. Tremor is also common after such lesions. The basal ganglia, doubtless, have important reflex functions, and comparative anatomy indicates that some functional relation exists between the lenticular nucleus and the arm; between the caudate nucleus and the leg. The effects of a lesion limited to any one of these ganglia, and producing no influence upon adjacent parts, are, however, beyond detection. As a matter of fact, seventy per cent. of the cases of hemiplegia are due to a lesion in the basal ganglia and affecting the internal capsule; and from the symptoms and nature of the disease its location there can usually be affirmed. The diagnosis is, however, made from the capsular symptoms, as already detailed.

IV. Lesions of the External Capsule and of the Claustrum cannot yet be located (Figs. 1010 and 1012). If on the left side, they usually produce parabhasia like the lesions of the island of Reil.

V. Lesions of the Corpora Quadrigemina are very rare. If the anterior pair is involved, blindness, loss of pupil reflex, strabismus, and nystagmus may be produced. If the posterior pair is involved disturbances of hearing and of coordination may be marked. As both pairs are usually affected together, the combination of these symptoms may aid a diagnosis. Blindness is such a common symptom of cerebral disease that it is only when it is not due to choked disc, optic atrophy, or neuritis, and when it is not of the nature of hemianopsia, that it is to be thought a local symptom of quadrigeminal lesion. A defective action of the same branches of the oculomotor nerves on both sides is rather more characteristic of quadrigeminal disease than the total affection of one nerve. In many cases of disease here ophthalmoplegia externa (*q.v.*) is the first symptom, and vertigo with incoordination of gait soon follows.

VI. Lesions of the Tegmentum of the Crura Cerebri, which lies beneath the corpora quadrigemina. Since the sensory tracts pass through this region, anesthesia may be produced by such a lesion, and the proximity of the corpora quadrigemina would give rise to indirect local symptoms of their affection. Lesions of the red nucleus cause the symptom of incoordination which occurs when the posterior pair of the corpora quadrigemina are involved. This is manifested by a staggering gait. They also cause paralysis of the third nerve, which passes through this nucleus. Lesions of the foot of the crus cerebri, in which the motor tract passes, cause hemiplegia of the opposite side. As the third nerve issues through the foot of the crus, a lesion here causes a paralysis of this nerve on the side of the lesion. Hence hemiplegia of one side, with third-nerve paralysis of the other side, indicates a lesion of the foot of the crus cerebri on the side of the third-nerve paralysis. This is called Weber's syndrome. Lesions on the base which press upon this part will produce the same combination of symptoms.

VII. Lesions of the Cerebellum, if located in the hemispheres and not in the median or vermiform lobe, and if of such a nature as not to exert pressure on surrounding parts, may not produce any symptoms. If the lesion is in the vermiform lobe, disturbances of coordination known as cerebellar ataxia occur, which consist in an inability to walk without staggering like a drunken man. The ataxia exists only while the patient is in an upright position; it rarely affects the motions of the arms, and when it does it never interferes with the fine adjustments, but only with extensive movements in space, *e.g.* grasping objects at a distance. These patients can stand with eyes closed without swaying. In these respects the ataxia differs from that of posterior sclerosis. A second characteristic symptom of cerebellar disease located in the vermiform lobe is vertigo. This may be very severe, but as it may occur without ataxia, and ataxia may be present without vertigo (though rarely), the two are not to be considered as interdependent. Vertigo is increased by rising to an erect position, but may persist when the patient is in bed. It decreases somewhat when the patient has remained fixed in any position for some time; but is always increased when he closes his eyes. The vertigo is usually an early symptom of cerebellar disease. It is more constant and persistent in cases in which the intracranial pressure is increased. It may gradually pass off in other cases. Cerebellar vertigo does not differ from vertigo in Ménière's disease, and is probably due to an affection of the terminal fibers of the eighth nerve, from the semicircular canals or their nuclei. The vertigo of Ménière's disease is, however, usually accompanied by deafness. Ataxia and vertigo together afford strong presumption of disease in the vermiform lobe, although neither alone is sufficient for a diagnosis. Nystagmus is a constant symptom of cerebellar disease and may be found on any movement of the eyes. The patient may not be aware of it. In cerebellar disease on one side, the head may be turned downward to the side of the lesion.

The indirect local symptoms of cerebellar disease may be numerous. They are due to an affection of the tracts and nerve nuclei in the pons and medulla (see Fig. 1009). Various forms of paralysis and anesthesia, vasomotor disturbances, obstinate vomiting of a projectile character, general symptoms of intracranial disease, *e.g.* headache, optic neuritis, are usually present with tumors, abscesses, or hemorrhages in the cerebellum, especially if they are in the median lobe. The combination of cerebellar ataxia and vertigo with these and other symptoms of pons disease (see Section IX.) affords clear evidence of disease in the cerebellum.

Lesions of the cerebellum have no apparent effect upon the mental powers when they occur in adults. A deficient development of the cerebellum is, however, a frequent cause of congenital idiocy. When one cerebellar hemisphere fails to develop, the opposite olivary body in the medulla and the opposite hemisphere of the cerebrum usually present an atrophic appearance.

Lesions of the middle peduncles of the cerebellum, the crura cerebelli ad pontem, produce characteristic symptoms. These consist in a tendency on the part of the patient to assume a forced position, to turn toward or fall toward one side in walking, or even to revolve constantly about one axis of his body. The forced movements may be made by the eyes (conjugate deviation in one direction), by the head,

or by the entire body. In a case seen by the writer, in which the autopsy showed a tuberculous tumor in the left middle peduncle and in the vermiform lobe, in addition to ataxia, vertigo, vomiting, and headache, the patient lay constantly on his left side, and when he turned upon his back or toward the right side the vertigo became so excessive that he was obliged to resume at once his former position. In walking, this patient showed a tendency to fall toward the right side, and found it impossible to turn around toward the right. Such patients may lose their balance in moving in one direction, *e.g.* forward or backward, and in attempting to regain it they may be obliged to hasten their movements. This has been interpreted wrongly as a tendency to compulsory walking in one direction, *e.g.* backward. It is

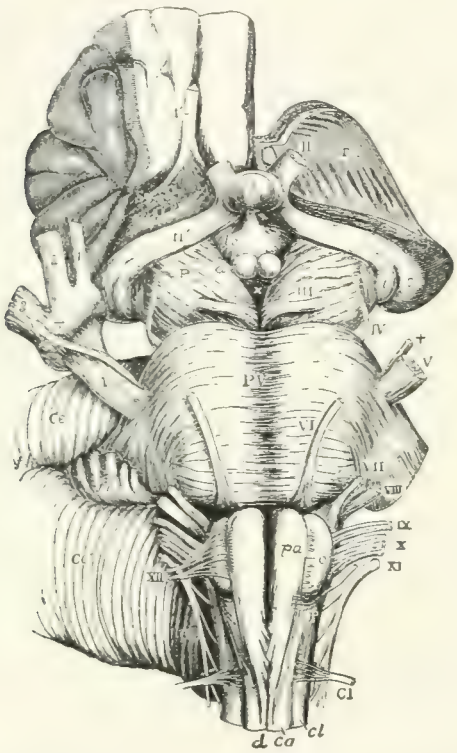

Fig. 1013.—The Base of the Brain and the Cranial Nerves. Pons and Medulla. *I* to *XII*, The cranial nerves; *Th*, optic thalamus; *h*, pituitary body; *tc*, tuber cinereum; *a*, corpora albicantia; *P*, pes pedunculi; *i*, internal, and *e*, external, geniculate body; *PV*, pons Varolii; *pa*, anterior pyramid of medulla; *o*, olive; *d*, decussation of anterior pyramids; *ca*, anterior column of spinal cord; *cl*, lateral column of spinal cord; *Ce*, cerebellum; *fl*, flocculus of cerebellum; *C1*, first cervical nerve.

really due to the vertigo. Lesions of the other peduncles of the cerebellum do not produce any known characteristic symptoms aside from those of cerebellar disease. It is to be remembered that the cranial nerves pass through or near the peduncles of the cerebellum and will necessarily be implicated in lesions there.

VIII. Lesions upon the Base of the Brain, tumors, chronic meningitis, may produce local symptoms by affecting the parts lying near them. Thus, all the cranial nerves may be involved either separately or in various combinations, and the nerve first or most severely affected may indicate where the lesion began. If such a lesion affects the optic nerve of one side, the optic chiasm, or the optic tract, blindness, either in the form of amaurosis of one eye or of hemianopsia of some variety, will be produced. If the lesion affects the crus cerebri or pons, the symptoms of lesion of this part (*vide supra* and Section IX.) may be present in addition to cranial-nerve paralysis. In all cases progressive bulbar paralysis and myasthenia gravis are to be excluded before the diagnosis is made. The local symptoms of lesion of those parts of the cortex which lie on the base of the skull are undetermined, but a tumor of some extent which invades the left Sylvian region may cause aphasia from pressure upon the island of Reil. The variety of symptoms possible in basal disease can be determined by the study of the organs upon the base of the brain, and any unusual combination of symptoms in intracranial diseases, especially if of syphilitic origin, should lead to a question as to the possibility of a lesion in this locality.

IX. Local Lesions in the Pons Varolii and Medulla Oblongata.—The pons Varolii and medulla oblongata lie upon the base of the brain, between the cerebrum and its crura above, the spinal cord below, and the cerebellum behind. Through them pass important tracts which join these organs with one another, and by means of which motor, sensory, vasomotor, and trophic impulses are sent from the brain to the body, and from the body to the brain. Diseases in the pons and medulla cause symptoms of wide extent and serious nature, by interfering with the transmission of these impulses. The pons and medulla are not, however, merely organs of transmission. They contain centers of great importance, and preside over numerous functions. In them are located the nuclei of origin of the cranial nerves from the fifth to the twelfth inclusive, and through them the cranial nerves pass outward from these nuclei to the surface. In them are also situated complex automatic centers, which preside over the acts of

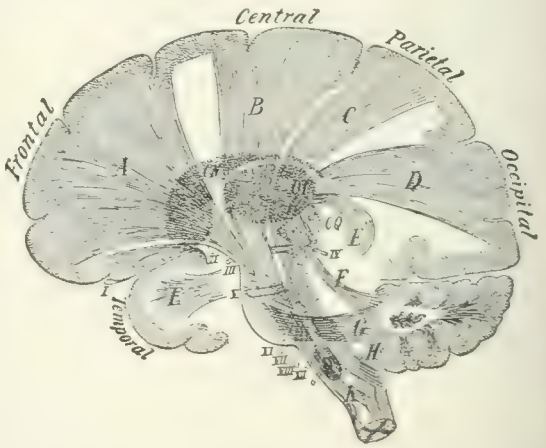

Fig. 1014.—The Projection Tracts Joining the Cortex with the Lower Nerve Centers. Sagittal section showing the arrangement of tracts in the internal capsule. The Roman numerals indicate the cranial nerves. References to the letters the same as in Fig. 1009.

combined movement of the eyeballs, deglutition, articulation, respiration, and cardiac inhibition, and which regulate the tone of the entire vasomotor system, and the secretion of saliva, perspiration, and urine. Disease in the pons and medulla, by affecting these various centers, produces important symptoms, and the complexity of those symptoms is evident from the number of normal functions which will be interfered with in any case of extensive lesion. These functions and their affections must be considered separately.

1. *The Tracts Passing through the Pons and Medulla.*—These may be studied by the aid of a schematic

drawing (Fig. 1018), and by comparing a number of sections made at different levels through the pons and medulla (Figs. 1015 to 1026).

(1) *Tracts Connecting the Cerebrum and Cerebellum* (Fig. 1014, A).—From the frontal lobe of each cerebral hemisphere tracts pass downward through the corona radiata, enter the anterior division of the internal capsule, and issue upon the base of the brain in the inner third of the pes pedunculi (Fig. 1015, *p*). From the parietal, occipital, and temporal lobes of each hemisphere tracts pass downward through the corona radiata, enter the posterior division of the internal capsule, and issue upon the base of the brain in the outer third of the pes pedunculi (Fig. 1015, *p*).

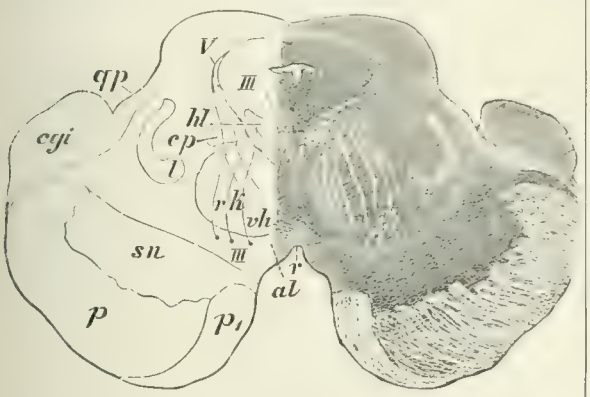

FIG. 1015.—Section through the Crura Cerebri. (Wernicke × 2.) *p*, Pes pedunculi; p_1, median fasciculus; *sn*, substantia nigra; *cgi*, corpus geniculatum internum; *qp*, corpus quadrigeminum posterior; *l*, lemniscus; *rk*, red nucleus of tegmentum through which pass fibers of oculomotor nerve, *III*, from its nucleus in the gray matter below the aqueduct of Sylvius, to its exit between the crura; *cp*, fibers in the formatio reticularis which have come from the posterior commissure; *hl*, posterior longitudinal bundle; *V*, descending root of the trigeminal nerve; *vh*, upper part of the decussation of the superior peduncles of the cerebellum, which end in the *rk*; *r*, raphé; *al*, lenticular loop.

A section through the crura cerebri at the level of the anterior corpora quadrigemina (Fig. 1015), shows the pes pedunculi ($p+p'$) separated from the tegmentum by the substantia nigra (*sn*).

The outer and inner thirds of each pes (exclusive of the median fasciculus p^1) are made up of these tracts from the cerebral lobes. After passing through the pes these tracts enter the pons Varolii, where they are split up into small bundles by the transverse fibers of the pons. Sections through the pons Varolii at various levels (Figs. 1016 to 1021) show that the basal half of the pons consists of longitudinal and transverse bundles of fibers interlaced, and that considerable masses of gray matter, consisting of large polygonal cells, lie between the fibers. It is in these gray masses that the longitudinal bundles under consideration from the cerebral lobes terminate. Hence, in the sections through the lower portion of the pons (Figs. 1020 and 1021), fewer longitudinal bundles are seen than in the upper sections. From the masses of gray matter in the pons, the transverse fibers originate and pass laterally to the cerebellum. The majority of the fibers from one-half of the pons pass to the opposite hemisphere of the cerebellum, and thus cross the median line, where they interlace with those of the other side. The gray masses of the pons are thus interposed in a continuous tract between the cerebrum and the cerebellum; each cerebral hemisphere being connected with both cerebellar hemispheres, but to a far greater extent with the opposite hemisphere than with the one upon the same side. Lesions of the frontal, parietal, and occipital lobes, if extensive, are followed by degeneration in the tracts from these lobes to the masses of gray matter in the pons. Congenital absence of the cerebral cortex (Porencephalie) results in congenital absence of these tracts. Absence or atrophy of the cerebellum is attended by absence or atrophy of the transverse fibers of the pons, which join the cerebellar hemisphere with the gray masses of the pons. Congenital deficiency of one cerebral hemisphere is occasionally attended by atrophy of the opposite cerebellar hemisphere, and *vice versa*. The function of the tract from the cerebrum to the cerebellum is doubtless to maintain a communication between these organs. But the exact function is unknown, and lesions in the course of these tracts in the pons do not produce any known symptoms.

(2) *The Motor Tracts.*—These enter the upper border of the pons from the middle third of each pes pedunculi (Fig. 1015), having come from the central convolutions through the corona radiata and anterior part of the posterior division of the internal capsule (Fig. 1014, B). Each motor tract, at its entrance into the pons, contains fibers whose destination is to the motor centers for the face, arm, and leg of the opposite side. But the centers of the facial nerve lie in the pons Varolii (Figs. 1020 and 1021). In its passage through the pons, therefore, the facial division of the motor tract leaves the remainder and crosses the median line. This crossing is made by way of the raphé, fibers leaving the longitudinal bundles in the ventral half of the pons, turning dorsad, entering the raphé, decussating with similar fibers from the opposite side, and then turning laterad to reach the facial nucleus (see Figs. 1020 and 1021). From the facial nucleus the facial nerve passes outward to the side of the pons, having first passed inward and curved around the abducens nucleus in

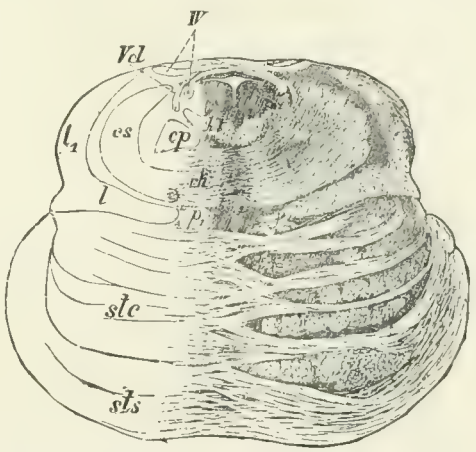

FIG. 1016.—Section through the Pons. (Wernicke, × 2.) *sts* and *stc*, Superficial and deep transverse bundles of fibers intersecting the longitudinal bundles, and terminating in the masses of gray matter of the basal portion; p_1, median fasciculus of the pes; *l*, lemniscus; l_1, lower lemniscus; *rk*, red nucleus of tegmentum; *cs*, superior peduncle of cerebellum, some fibers of which are decussating in the raphé; *cp*, fibers in formatio reticularis, which have come from the posterior commissure; *hl*, posterior longitudinal bundle; *Vd*, descending root of the fifth nerve; *IV*, fourth nerve decussating in the valve of Vieussens.

the so-called knee of the facial nerve. The accompanying diagram indicates the course of the motor tract in the pons and medulla. As a result of the division of the motor tract of one side, lesions in the pons produce different forms of paralysis, according to their location. A lesion in the motor tract in the upper third of the pons causes hemiplegia of the side opposite to the lesion (Fig. 1018, lesion at *A*). A lesion in the middle or lower third of the pons causes alternating paralysis, *i.e.* paralysis of the face on the side of the lesion, with paralysis of the arm and leg

on the opposite side (Fig. 1018, lesion at *B*). In the first case (hemiplegia) the upper branch of the facial nerve is not affected, the patient can close his eye on the paralyzed side, and the facial muscles contract

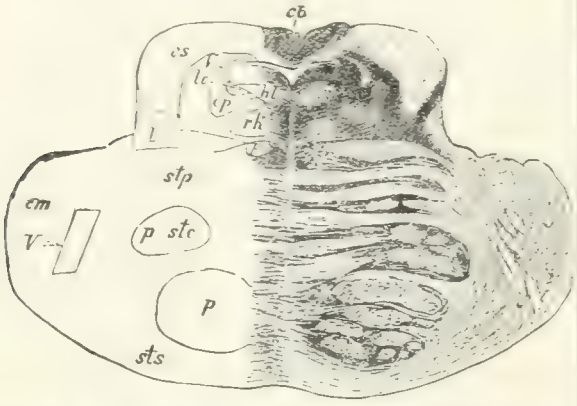

FIG. 1017.—Section through the Pons. (Wernicke, × 2.) *sts*, *stp*, *stp*, Superficial and deep transverse bundles of the pons, intersecting the longitudinal bundles, and terminating in the mass of gray matter of the basal portion; *p*, pyramidal (motor) tract from the middle third of the pes; p^1, median fasciculus of the pes, here seen to join the lemniscus, *l*; *V*, fifth nerve root; *cm*, middle peduncle of cerebellum; *cs*, superior peduncle of the cerebellum with *cb*, valve of Vieussens; *rk*, *hl*, *cp*; *lc*, locus ceruleus.

to the faradic electric current. In the second case (alternating paralysis) all branches of the facial nerve are involved, the eye remains open, and the reaction of degeneration develops soon after the lesion occurs. In this case it is usual to find a paralysis of the abducens nerve on the same side as the facial paralysis, in which case the eyeball will be turned in.

The motor fibers to the tongue take a similar course to those to the face, but leave the motor tract at a point in the lower third of the pons. Having reached the hypoglossal nucleus in the medulla they end, but the hypoglossal nerve passes outward, lying in close proximity to the motor tract in the medulla, as shown in the diagram. A lesion in the lower third of the pons or in the medulla may thus cause paralysis of one side of the tongue and of the opposite arm and leg (Fig. 1018, lesion at *C*). In the medulla the motor tracts pass in the anterior pyramids (see Fig. 1013, *pa*), and before entering the spinal cord undergo partial decussation. A lesion in one pyramid will cause paralysis of the opposite arm and leg (Fig. 1018, lesion at *D*); but as the two pyramids lie side by side, lesions of the medulla, by affecting both at once, may produce paralysis of both arms and legs; and this is especially the case if the lesion lies so near the spinal cord as to involve the decussation (Fig. 1018, lesion at *E*).

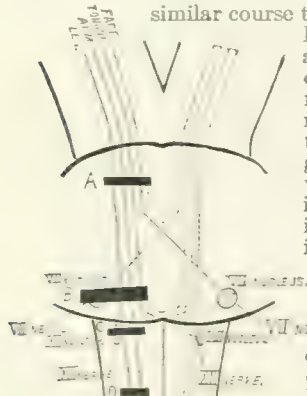

FIG. 1018.—The Motor Tract in [illegible] causes hemiplegia of side opposite to lesion; lesion at *B* causes alternating paralysis; lesion at *C* causes paralysis of tongue on side of lesion and of extremities of opposite side; lesion at *D* causes paralysis of extremities of opposite side; lesion at *E* causes paralysis of extremities of both sides.

The various forms of paralysis produced when both sides of the pons are involved at once can be ascertained by reference to the diagram.

In all these affections of the motor tract a condition of spastic rigidity may follow the paralysis, and an increase of tendon reflexes is usually observed. In a few cases of pons lesion, however, the tendon reflexes have been lost. The electric condition of the paralyzed muscles in the limbs is normal from the outset, and no rapid atrophy occurs.

The situation of the pyramidal tract is seen in all the figures at *p*. In the upper part of the pons (Figs. 1016 and 1017) its fibers are seen to be split up into small bundles by the transverse pons fibers. In the middle of the pons, however (Fig. 1019), they have collected together, and in the lower part of the pons (Figs. 1020 and 1021) they form a compact tract which continues downward in the anterior pyramid of the medulla (Figs. 1022 to 1025, *p*). At the lowest level of the medulla (Fig. 1025) the pyramidal fibers decussate, and thus pass into the lateral columns of the spinal cord. About one-fifth of the pyramidal fibers do not, however, take part in the decussation, and these continue downward in the anterior median columns of the spinal cord. The ratio of decussating to non-decussating fibers was found by Flechsig to vary greatly, and in one case in sixty no decussation occurs. The relative sizes of one lateral pyramidal tract and of the opposite anterior median column of the spinal cord depend wholly upon the extent of the decussation of the pyramids in the medulla.

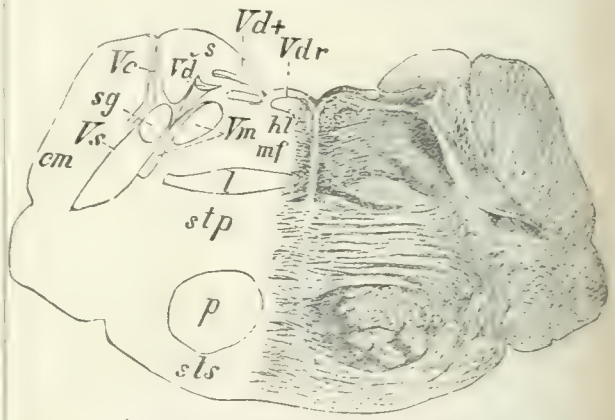

FIG. 1019.—Section through the Pons. (Wernicke, × 2.) [illegible] Superficial and deep transverse pons fibers from the cerebellum through *cm*, the middle cerebellar peduncle; *p*, the pyramidal (motor) tract; *l*, lemniscus; *mf*, formatio reticularis; *hl*, posterior longitudinal bundle; *Vm*, motor nucleus and root of the trigeminal nerve; *Vs*, sensory root of the trigeminal nerve; *Vc*, cerebellar root of the trigeminal nerve; *Vd*, descending root of the trigeminal nerve; *Vd+*, crossed descending root of trigeminal nerve; *Vdr*, fibers from the raphé to the trigeminal root; *sg*, substantia gelatinosa of *V* root.

(3) *The Tract of Muscular Sense.*—This is called the lemniscus or fillet in the pons, and the interolivary tract in the medulla. As it conveys sensations upward we trace it in that direction. It arises from the nuclei gracilis and cuneatus on the dorsal surface of the medulla, in which the columns of Goll and Burdach of the spinal cord end (Figs. 1025 and 1026, *ft* and *fc*). It then crosses the median line, decussating with its fellow of the opposite side in the upper decussation of the medulla (sensory decussation of Meynert; pinniform decussation of Spitzka) (Fig. 1025, *l*, *ft*). The fibers after decussating turn upward, enter the interolivary tract, and pass onward through the medulla beyond the upper level of the olives into the pons (Figs. 1022 and 1023, *l*). Here this tract broadens out, becoming almost ribbon-like in its appearance, and hence has been called the fillet. In

the pons the fillet lies behind the deep transverse bundles of the pons, and just in front of the formatio reticularis (see Figs. 1016 to 1021, *l*).

As it passes up it receives additional fibers from the superior olive (Fig. 1022, *o*, *s*), but these leave it again at the level of the posterior corpora quadrigemina (Fig. 1016, *l*'), while the main part of the fillet passes onward in the outer part of the tegmentum of the crus cerebri (Fig. 1014, *l*), and thence into the posterior part of the internal capsule, whence it radiates to the parietal cortex of the brain.

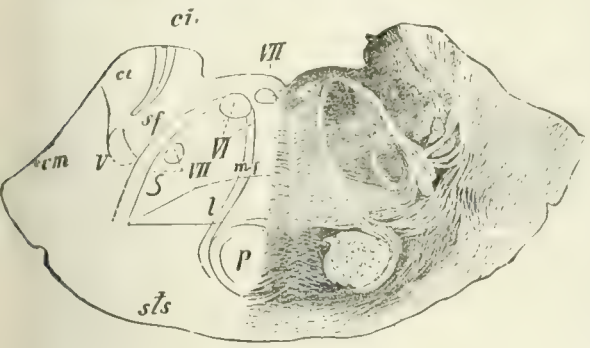

Fig. 1020.

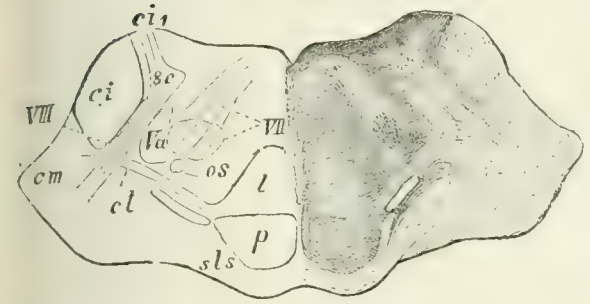

Fig. 1021.

Figs. 1020 and 1021.—Sections through Pons. (Wernicke, × 2.) *sts*, Superficial transverse pons fibers from cerebellum through *cm*, middle cerebellar peduncle; *p*, pyramidal tract; *l*, lemniscus; *mf*, formatio reticularis; *VI*, abducens nucleus from which abducens nerve passes forward, lying near *p*; *VII*, facial nucleus lying deep in *mf*, sending its fibers backward toward the floor of the ventricle (Fig. 1020), where they turn upward (Fig. 1021), and then curve outward, thus forming a bend or knee around the *VI* nucleus; *Va*, ascending root of trigeminal nerve; *ci*, inferior cerebellar peduncle; *VIII*, auditory root; 8*c*, external auditory nucleus; *ct*, corpora trapezoidea; *os*, superior olive.

Sensations of muscular sense being transmitted by this tract, a lesion in it causes ataxia in the limbs of the opposite side. A unilateral ataxia may indicate a lesion in the course of the fillet.

(4) The *Sensory Tract*, which transmits sensations of touch, temperature, and pain through the medulla and pons, is in the formatio reticularis. This portion of the medulla and pons lies just beneath the gray matter of the floor of the fourth ventricle, behind the tracts hitherto described. It is made up of nerve fibers passing in three directions: (*a*) transversely, the commissural fibers of the cranial nerve nuclei; (*b*) from the nuclei ventrad, the fibers of the cranial nerve roots and arciform fibers; (*c*) longitudinally, the sensory tract. The longitudinal fibers can be traced from the gray matter and various columns of the spinal cord, through the formatio reticularis to its upper level in the tegmentum of the crus, whence they issue to enter the posterior part of the internal capsule. In the medulla the formatio reticularis of each side is divided into two parts by the line of exit of the nerve roots of the twelfth (see Fig. 1023). The inner part, near the median line, contains the continuation of the anterior and antero-lateral columns of the spinal cord, and the interolivary tract or lemniscus already described. The outer part contains the sensory tract now under consideration. In the inner two-thirds of this outer part the fibers pass which convey impressions of touch, temperature, and pain from the opposite half of the trunk and limbs. In the outer third of this part is found a column of peculiar structure resembling the substantia gelatinosa of the posterior horn of the spinal cord, and in this column terminate the fibers of the sensory part of the trigeminal nerve (Figs. 1022 and 1023, *Va*), which turn downward after entering the pons Varolii, and terminate at different levels in the pons and medulla (see Fig. 1024). Thus the outer portion of the formatio reticularis contains the sensory tract from the face of the same side. It is evident from the diagram that a lesion which involves one-half of the formatio reticularis in the pons and medulla will produce an alternating anesthesia, *i.e.* loss of sensation on one side of the body and on the other side of the face and head (lesion at *B*, Fig. 1024). Alternating anesthesia is as characteristic a symptom of lesions of the formatio reticularis of the pons and medulla, as alternating paralysis is of lesions in the motor tract of the pons. In the upper part of the pons the sensory tract from the face crosses the median line, and hence a lesion in the formatio reticularis in the upper third of the pons, or in the crus cerebri, will produce a unilateral anesthesia (lesion at *A*, Fig. 1024; see Fig. 1019, *Vdr*, *Vd*+). A lesion involving both halves of the formatio reticularis will produce bilateral sensory symptoms.

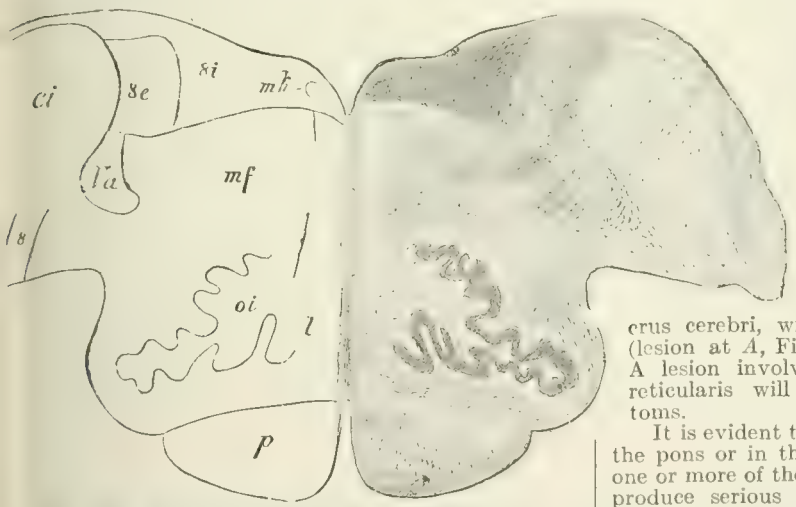

Fig. 1022.—Section through Medulla. (Wernicke, × 4.) *p*, Pyramid; *l*, lemniscus or interolivary tract; *o*, olive; *mf*, formatio reticularis; *Va*, ascending root of trigeminal nerve; 8, auditory root; 8*e*, external auditory nucleus; 8*i*, internal auditory nucleus; *mk*, upper end of hypoglossal nucleus; *ci*, inferior peduncle of cerebellum.

It is evident that a lesion of any extent, either in the pons or in the medulla, will inevitably destroy one or more of these four tracts, and consequently will produce serious symptoms of wide extent and of considerable diversity.

2. *The Centers Lying in the Pons and Medulla.*—The cranial-nerve nuclei lying in the pons and medulla must be briefly enumerated, since lesions affect them. They are located either in the gray

matter of the floor of the fourth ventricle, or below this in the formatio reticularis.

Figs. 1027 and 1028 show the relative position of the cranial-nerve nuclei in the pons and medulla from the fifth to the twelfth, inclusive.

The third and fourth nerve nuclei and roots, together with the effect of lesions in them, will be discussed in the article on *Ophthalmoplegia*.

The cranial nerves from the fifth to the twelfth

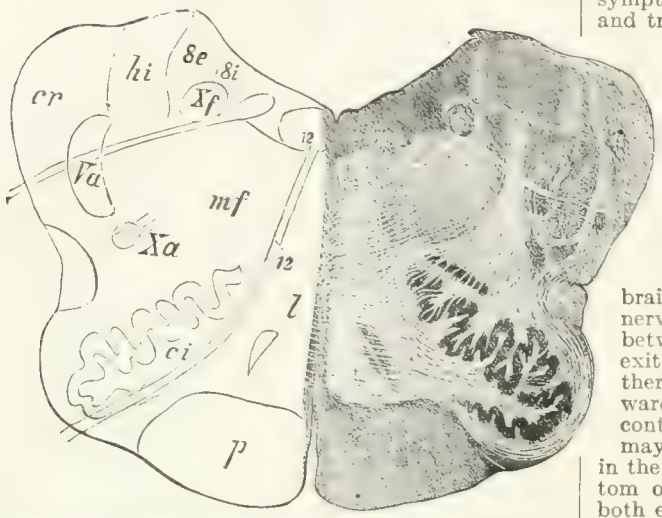

FIG. 1023.—Section through Medulla. (Wernicke. × 4). *p*, Pyramid; *l*, lemniscus or interolivary tract; *ci*, fibers from the olive which cross the raphé and pass outward and backward to enter the inferior cerebellar peduncle, *cr*; *mf*, formatio reticularis, in which *Xa*, the deep nucleus of the vagus (nucleus ambiguus), lies; *Va*, ascending root of trigeminal nerve; 12, hypoglossal nucleus and root; *Xf*, respiratory bundle around which, in the floor of the ventricle, the vagus nucleus lies, and below which the vagus root issues; *8e* and *8i*, auditory nuclei; *hi*, nucleus cuneatus, from which fibers pass outward and enter *cr*.

may be considered in two categories: first, the motor nerves; second, the sensory nerves.

(1) The *Motor Nerves* are the motor branch of the trigeminal which supplies the muscles of mastication, the abducens, the facial, the motor portion of the glosso-pharyngeal and of the vagus, the spinal accessory, and the hypoglossal.

Lesions which irritate the tracts from the cortical centers to these nuclei, or lesions in their vicinity which cause irritation, may produce spasm of the muscles supplied by them. Thus spasm of the jaw (trismus), with grinding of the teeth, nystagmus, conjugate lateral deviation of the eyes, spasm of the face, spasm of the throat and larynx, and spasm of the tongue may occur from lesions of an irritating nature. Such are small hemorrhages, small areas of softening, or small tumors in the pons or medulla. Such lesions must lie in or near the floor of the fourth ventricle, or in the course of the nerve roots, to produce these spasms. A review of recent literature shows that they are to be regarded as rare symptoms. If such spasms occur alone, without other symptoms, it is difficult to determine the nature of the lesion, or to decide that the spasm is not functional. If they occur in connection with other symptoms of pons or medullary lesion, they are valuable as evidence oi the exact position of the disease.

Lesions which interrupt the tracts from the cortical centers to the motor-nerve nuclei, which destroy those nuclei, or which interfere with the conduction of impulses along the nerve root and nerve trunk, will produce paralysis. Paralysis of the muscles of mastication is the rarest form of paralysis. Paralysis of the external rectus muscle, or of the facial muscles and tongue, is very common. Paralysis of deglutition or of the vagus is occasionally met with. It is easy to determine in any case whether the paralysis is due to lesion of the central tracts, or to lesion of the nerve nuclei. In the first case atrophy does not follow the paralysis, and there is no change in the electric reaction in the muscles. In the second case atrophy occurs soon after paralysis, and is accompanied by a reaction of degeneration. But the latter symptoms are common to lesion of the nerve root and trunk as well as to lesion of the nucleus; hence other symptoms are necessary to establish a diagnosis of a lesion in the nucleus. When paralysis of the muscles supplied by one cranial nerve occurs alone, the probability is in favor of a peripheral nerve lesion, *e.g.* a meningitis or tumor on the base of the brain; and a central lesion can be thought probable only when an implication of other muscles in the domain of other nuclei ensues.

Paralysis of the external rectus is so common that it requires some attention. It is usually due to a lesion on the base of the brain outside of the pons, involving the sixth nerve. It may be due also to lesion in the pons between the nucleus of the sixth nerve and the exit of the root (see Fig. 1020). In both cases there will be a permanent deviation of the eye inward and an inability to turn it outward, with contraction of the pupil. But abducens paralysis may also be due to a lesion of the abducens nucleus in the pons. In such cases there is the added symptom of inability to perform conjugate movement of both eyes toward the side of the lesion, and a permanent deviation of both eyes to the opposite side. But this deviation does not prevent the voluntary act of convergence of both eyes to a near point. Lastly, abducens paralysis may be due to lesions in the crus, or between the crus and the cortex, in the course of the tract conveying voluntary impulses from the cortex to the sixth-nerve nucleus. Such lesions will interfere with voluntary conjugate movement of both eyes to one side, viz., toward the side whose abducens is paralyzed. But since such a lesion may lie in the pons after the decussation of this tract, or in the cerebrum before its decussation, it cannot be said that the deviation is uniformly either toward or away from the lesion. In this case there is no permanent deviation of the eyes to either side; for the abducens nucleus being uninjured, it maintains the tone of the external rectus muscle, and during rest the eyes are found directed forward. If a lesion in the course of the central tract is of an irritative nature, however, it may cause forced motions of the eyes by sending impulses to the sixth nucleus. Under these circumstances there will be conjugate deviation of both eyes toward the side of the abducens paralysis.[1]

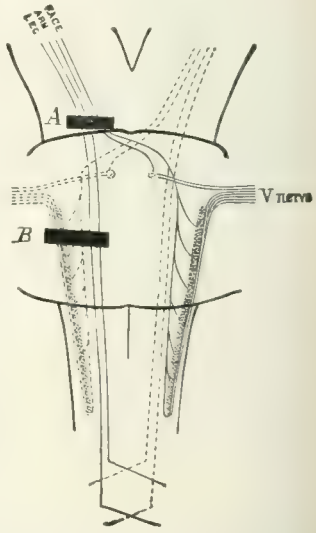

FIG. 1024.—The Course of the Sensory Tract in Pons and Medulla. *A*, Lesion in tegmentum of crus cerebri, or upper quarter of pons, producing hemianesthesia of the opposite side; *B*, lesion in formatio reticularis of pons or medulla, producing alternating anesthesia.

The act of conjugate movement may also be interfered with, without paralysis of the abducens nerve. That act is governed by the sixth nerve nucleus, or by a special nucleus in its immediate vicinity as yet undetermined. It involves an innervation of one external rectus muscle and of the opposite internal rectus muscle. But the internal rectus muscle derives its innervation from the third nerve. A crossed connection must therefore be maintained between the abducens of one side and the oculo-motorius of the other side. This connection is maintained by means of the posterior longitudinal fasciculus (Figs. 1015 to 1021, *hl*). A lesion in the pons in the course of this bundle will interfere with the act of conjugate movement without paralyzing either abducens or oculomotor nerve alone. In none of the cases mentioned is voluntary convergence of the eyes to a point suspended. These conditions may be understood by reference to Fig. 1029.

A very extreme contraction of the pupils is mentioned as a symptom in cases of sudden lesion of the pons. It has not been explained.

Paralysis of the facial muscles is very common, but is usually due to lesions in the nerve outside of the pons. The symptoms which are produced when the facial nerve root or its nucleus is invaded in the pons, resemble those of Bell's palsy; for all the facial muscles are affected, and an atrophy with reaction of degeneration ensues. The situation of the lesion in the pons can be determined only when other symptoms of pons disease, such as alternating paralysis (Fig. 1018), are present.

Paralysis of the motor portion of the glosso-pharyngeal nerve, with dysphagia or difficulty of swallowing, is a not infrequent symptom of pons disease. It occurs after sudden lesions, such as hemorrhage or embolism, also as the result of tumors, and most

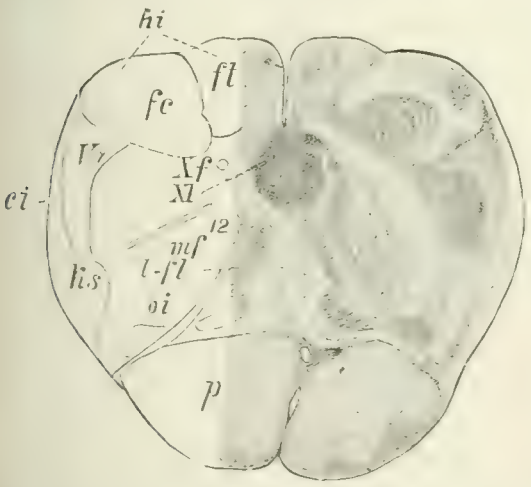

Fig. 1025.—Section through Medulla, Level of Sensory Decussation. (Wernicke, × 4.) *ft*, Nucleus gracilis; *fc*, nucleus cuneatus, from which fibers curve around the central gray, and then decussate and turn upward (cephalad) in the interolivary tract, *l-ft*; *Va*, ascending root of the trigeminal nerve; *ci*, inferior peduncle of cerebellum, of which *ks*, direct cerebellar column of the cord, is a part; *Xf*, respiratory bundle; *XI*, medullary nucleus of spinal accessory nerve and its root; 12, hypoglossal nucleus and root; *mf*, formatio reticularis; *oi*, olive.

frequently of all in progressive bulbar paralysis. It is to be remembered that in myasthenia gravis which is a functional disease probably due to a toxin the early symptoms are seen in affections of the muscles supplied by the cranial nerves. The variability of the symptoms and recovery under rest will enable the physician to differentiate this disease from bulbar paralysis.

Paralysis of the motor and vasomotor mechanisms, governed by the vagus nerve, is a constant symptom of disease in the lower part of the pons and in the medulla. Arrest of respiration and heart action, from lesion of this nucleus, is the cause of sudden death, which so frequently attends sudden lesions in the medulla and pons. When the lesion is, however, of a slowly progressive nature (tumor, sclerosis about

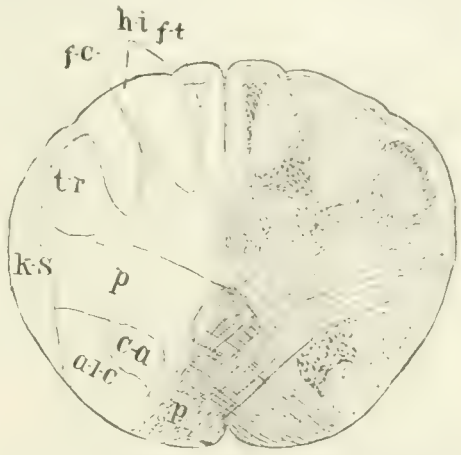

Fig. 1026.—Section through Medulla, Level of Motor Decussation. *hi*, Posterior columns of spinal cord; *ft*, nucleus gracilis in column of Goll; *fc*, nucleus cuneatus in column of Burdach; *tr*, tubercle of Rolando, where posterior horn of spinal cord merges into *Va*, ascending root of *V*; *ks*, direct cerebellar column; *p*, pyramid decussating to reach lateral column; *ca*, anterior cornu of cord; *alc*, anterolateral column of cord.

a hemorrhage), symptoms of irritation may occur from gradual invasion of the pneumogastric centers. Projectile vomiting; slow or very rapid, or intermittent, irregular pulse; dyspnea; loss of voice; polyuria and glycosuria, are symptoms which have been ascribed to such lesions. The two last-named symptoms have been associated with tumors in the lower part of the medulla[2] and upper part of the spinal cord, which have involved the fibers from the vasomotor center on their way downward to their exit from the cord at the eighth cervical segment. The intramedullary nucleus of the spinal accessory nerve is so closely adjacent to that of the vagus that they are usually involved together, when difficulty of respiration and articulation ensues. When the spinal portion of the nerve is affected, spasms of the neck occur; but this symptom is characteristic of meningeal affections, and has not been observed in central lesions.

An affection of the hypoglossal nerves or their nuclei is very frequently observed in medullary disease, partly because the nerves pass through the middle of the medulla, and partly because their nuclei are large. If the lesion produces irritation of one nucleus, fibrillary twitchings and spasm in one-half of the tongue may be caused. It is more usual to find paralysis than spasm, in which case the tongue, when protruded, will deviate toward the paralyzed side, and will, therefore, point toward the lesion. But when the tongue is affected by disease in the medulla, it is not unusual for both halves to be involved, and then it is found that the power of protruding it is suspended, and motions in the mouth are also difficult. Hence talking, chewing, and swallowing are interfered with. An electric examination in these cases will demonstrate the reaction of degeneration in the intrinsic muscles of the tongue, and prove that the lesion is medullary, and not cerebral. Anarthria or dysarthria, *i.e.* imperfect articulation, is, according to Nothnagel, a frequent and important symptom of medullary disease.

(2) The *Sensory Nerves* of the pons and medulla are the trigeminal, the auditory, and the glosso-pharyngeal. Lesions which affect the trigeminal nerve and produce anesthesia of the face have already been considered. Trophic disturbance of the eyeball has not yet been observed in cases of lesion of the trigeminal root or nucleus. The auditory nerve is occasionally affected in diseases of the pons and medulla. Two sets of symptoms are then produced: one referable to the implication of the fibers conveying auditory impressions, the other due to the irritation or destruction of fibers concerned in the sense of equilibrium. Deafness has been observed in pons

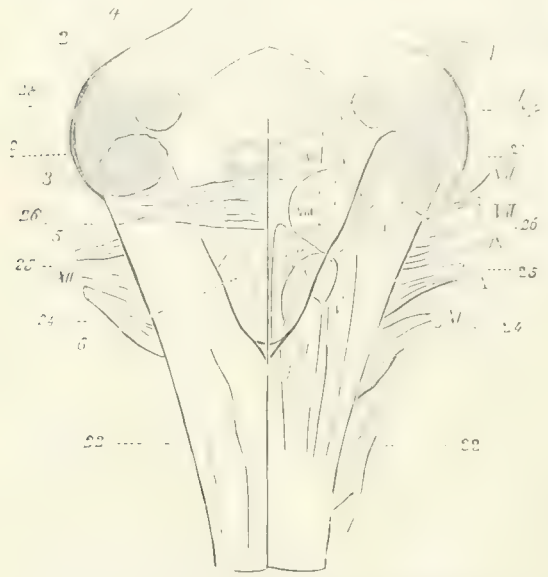

FIG. 1027.—Diagram Showing the Position of the Cranial Nerve Nuclei upon the Floor of the Fourth Ventricle (Erb). *v* to *xii*, Nuclei; *V* to *XII*, cranial nerves; *v*, median of *V*; *v'*, motor nucleus of *v''*, ascending root of *V*; *viii*, inner nucleus of *VIII*; *viii'*, outer nucleus; *viii''*, *viii'''*, lateral nuclei of *VIII*; 27, middle cerebellar peduncle; 3, inferior cerebellar peduncle; 2, superior cerebellar peduncle; 4, eminentia teres; 5, striæ acusticæ; 6, ala cinerea.

disease on the side of the lesion,[3] and is probably due to destruction of the auditory fibers passing inward to the inner auditory nucleus on the floor of the fourth ventricle, or to an implication of that nucleus (see Fig. 1022). The central course of the auditory tract is believed to be as follows: From the inner and outer auditory nuclei fibers cross the median line in the corpus trapezoides (Fig. 1021, *ct*) to the opposite superior olive, thence turn

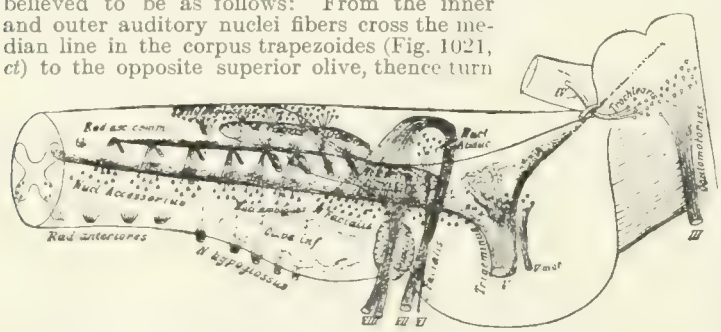

FIG. 1028.—Longitudinal Section Showing the Relative Position of the Cranial Nerve Nuclei (Edinger).

upward with the lemniscus, pass beneath the posterior corpora quadrigemina in the lower lemniscus (Fig. 1015, l^1), and thus reach the internal geniculate body, from which a tract passes outward through the lower posterior part of the internal capsule and corona radiata to the temporal lobe of the brain (Figs. 1014, 1022). The course of this tract has been traced by anatomists, and has been confirmed by pathological observation. Lesions at any part of it

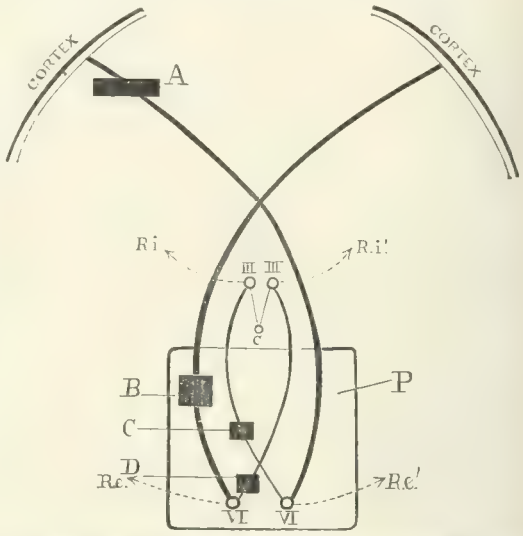

FIG. 1029.—The Innervation of the Muscles of the Eye. (After Hunnius, "Zur Symptomatologie der Bruckenerkrankungen.") P Pons Varolii; III, oculomotor nuclei, with R.i., nerve to left internal rectus, and R.i.', to right internal rectus; VI, abducens nuclei, with R.e., nerve to left external rectus, and R.e.', to right external rectus; tract from cortex to VI conveys voluntary impulses of conjugate deviation of the eyes; tract from VI to III unites the action of one external rectus with the opposite internal rectus; *C*, center for convergence of the eyes which is independent of VI and is actually in connection with the cortex by independent tracts not shown; A, situation of a lesion in the cerebrum producing loss of voluntary conjugate deviation of the eyes to the right; B, situation of a lesion in the pons producing loss of voluntary conjugate deviation of the eyes to the left; C, situation of lesion in the pons in the posterior longitudinal bundle, causing paralysis of conjugate motion to the right; D, situation of a lesion in the pons in the posterior longitudinal bundle, and involving the VI nucleus, causing loss of conjugate motion to the left, with permanent deviation of the eyes to the right.

should produce deafness in one ear. Disturbance of equilibrium may occur from lesions in the lateral portion of the pons, if such lesions interrupt the part of the auditory nerve conveying such sensations to the cerebellum. This part of the auditory nerve passes either directly into the cerebellum through the inferior peduncle, or terminates in the external auditory nucleus, which is connected by fibers with the cerebellum (Figs. 1020, 1021, *e*, ci^1). Vertigo, which is a frequent symptom of pons lesion, and rotatory movements of the body toward one side, which is an occasional symptom of pons disease when the lesion involves the lateral portion of the pons, and the inferior and middle cerebellar peduncles, are probably due to an involvement of this portion of the auditory nerve in the lesion. The rotatory movement is probably due to a voluntary attempt to correct a subjective sense of motion. The patient really suffers from vertigo, and thinks that he is turning or falling toward one side; he therefore tries to prevent this falling by turning toward the other side. The symptom may be so serious that such rotatory movements are constantly kept up until the patient dies of exhaustion. The patient turns toward the side opposite the lesion (?).

The sensory portion of the glosso-pharyngeal nerve receives the sensations of taste, and in two cases in which its nucleus has been involved a loss of taste has occurred. This symptom is so rarely elicited that it is not known whether lesions elsewhere in the pons or medulla will produce it.

The Vasomotor Center.—Lesions in the upper half of the medulla produce marked vasomotor symptoms. They consist of a general vasomotor paralysis with flushing of the surface and sensation of heat, and of abnormal sweating. The vasomotor center is bilateral, and each center controls the circulation on the same side of the body. Lesions in its area are so likely to cause sudden death that but few cases can be found in which it was affected (eight cases in my collection). But the symptoms of a vasomotor character are to be looked for in any case of medullary lesion, and when such symptoms are limited to one lateral half of the body, and are associated with other symptoms of bulbar disease, they are valuable as signs of the situation of the lesion.

There are a few general symptoms that have been not infrequently observed in pons disease which require mention. General convulsions are the most constant of these. The majority of sudden lesions (hemorrhage, embolism) in the pons are ushered in by general convulsions, followed by coma. Nothnagel established the fact that in animals irritation of the pons produces general convulsions, and hence authors have spoken of a convulsive center in the pons. It is hardly warrantable to hypothecate such a center. But it is probable that lesions in the pons are capable of producing general convulsions by irritating the motor tracts which pass through it. This is borne out by the fact that when the lesion is a tumor or a sclerosis, *i.e.* a gradually increasing lesion, convulsions do not occur. Headache, disturbance of vision, vertigo, and psychical changes have been frequently observed in connection with diseases of the pons and medulla, but they are to be ascribed to changes in the circulation or internal cranial pressure, and not to any special local lesion.

It is evident from this review that the symptoms of lesions of the pons and medulla are very numerous, very complex, and very various, in accordance with their extent and the manner of their occurrence. The symptoms in bulbar paralysis are very different from those of softening from embolism. And as almost every case so far recorded has differed from every other in important particulars, it is necessary to study carefully and fully all the symptoms occurring in any case of central lesion. If the cranial nerves are involved, or if there is present alternating paralysis or anesthesia, the possibility of pons or medullary disease must be considered, and an investigation of the various symptoms here detailed should not be neglected.

M. Allen Starr.

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Brain, Growth of the.—The following article aims to give a general account of the growth changes which occur in the human brain and cord, between birth and the natural end of life, thus including those found in old age. As the interest in these changes arises mainly from the relations of growth to functional development, it is customary to discuss also some changes which are related to age but which cannot be called growth changes in the strict sense. Thus we have the structural alterations in the neurone from birth to maturity—some of which at least are not associated with an increase in size—so too alterations of the neurones in old age are considered though these are usually accompanied by a decrease in size. Finally, there are certain intracellular and chemical modifications during the life cycle which as yet we are unable to associate directly with changes in size. To make the discussion significant therefore the field covered must be somewhat broader than that indicated by a strict interpretation of the title.

Two main conditions control the growth changes in the nervous system: nutrition and time (age). In many instances the relative importance of these two has still to be determined, but we may safely say at the present moment that the growth process in the strict sense (*i.e.* increase in size) readily responds to variations in nutrition while intracellular differentiation and chemical modification are more evidently correlated with time (age).

In discussing the changes which occur in the neuraxis (brain and spinal cord—central nervous system), the following outline will be employed:

(A) Growth changes in the neuraxis:
  (1) Brain,
  (2) Spinal cord.
(B) Percentage of water.
(C) Growth changes in the neuraxis considered as the resultant of changes in the cells which constitute it:
  (1) Number of neurones,
  (2) Size of neurones.
(D) Growth changes in the cerebral cortex.
(E) Changes during old age.
(F) Summary.

A. Growth Changes in the Neuraxis. 1. *Brain.*—The human encephalon varies widely in weight at maturity, even when members of the same race and the same social class are alone compared. Differences in the final weight must be looked upon as resulting from differences in the process of growth acting on the number of constituent elements present at birth. In all probability this number is not subject to any considerable individual variation in normal persons. The weight of the encephalon at maturity is illustrated by the accompanying table based on the observations of Dr. Boyd.

Table I.—Showing in Grams the Weight of the Encephalon and Its Subdivisions in Sane Persons, the Records Being Arranged According to Sex, Age, and Stature. (From Marshall's tables, 1892, based on Boyd's records (1861).

Sane.

Males.					Females.				
Ages.	Encephalon.	Cerebrum.	Cerebellum.	Stem.	Stem.	Cerebellum.	Cerebrum.	Encephalon.	Ages.
Stature 175 cm. and upward.					Stature 163 cm. and upward.				
20–40	1409	1232	149	28	23	134	1108	1265	20–40
41–70	1363	1192	144	27	23	131	1055	1209	41–70
71–90	1330	1167	137	26	24	130	1012	1166	71–90
Stature 172-167 cm.					Stature 160–155 cm.				
20–40	1360	1188	144	28	26	137	1055	1218	20–40
41–70	1335	1164	144	27	26	131	1055	1212	41–70
71–90	1305	1135	142	28	24	128	969	1121	71–90
Stature 164 cm. and under.					Stature 152 cm. and under.				
20–40	1331	1168	138	25	24	130	1045	1199	20–40
41–70	1297	1123	139	25	25	129	1051	1205	41–70
71–90	1251	1095	131	25	25	123	974	1122	71–90

These records were obtained from 2,086 patients of the Marylebone Workhouse in London, representing, for the most part, the least favored class of persons

native to Great Britain. For the purpose of weighing, the encephalon was divided into three portions: (1) The cerebrum, including all parts frontal to the midbrain; (2) the cerebellum, severed at the peduncles; and (3) the stem—the midbrain, pons, and bulb.

Owing to the fact that these records are based on a workhouse population, it is probable that they represent brains less well grown and earlier subject to senile atrophy than would be the case among the more prosperous members of the community. In any other corresponding series the general relations to which we are about to call attention would, however, remain the same.

In comparing the sexes Table I. shows that the heavier brains belong to the males; on comparing those of different stature within each sex, that they belong to the tall individuals; and when those of the same sex and stature are compared, according to age, to those in the prime of life, *i.e.* twenty to forty years of age. The only exception to this statement is found in the 40–70 years group of shortest females. Sex and stature, then, are conditions which modify the weight which the brain will attain at maturity, and after the prime of life its weight diminishes.

Having indicated the weight at maturity under the conditions of the race and social class here chosen, we have next to determine the weight of the encephalon at birth, and the course of the changes by which it reaches its full size. Vierordt (1890) has collected the most complete series of observations for the change in brain weight between birth and twenty-five years of age. The data are taken mainly from German records. They are printed in Table II.

Table II.—To Show the Increase in Brain Weight with Age. Encephalon Weighed Entire with Pia.

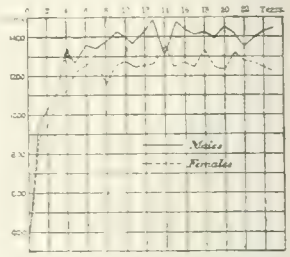
Age.	Males.		Females.	
	Number of cases.	Brain. Grams.	Number of cases.	Brain. Grams.
0 months..	36	381	38	384
1 year.....	17	945	11	872
2 years...	27	1025	28	961
3 years...	19	1108	23	1040
4 years...	19	1330	13	1139
5 years...	16	1263	19	1221
6 years...	10	1359	10	1265
7 years...	14	1348	8	1296
8 years...	4	1377	9	1150
9 years...	3	1425	1	1243
10 years...	8	1408	4	1284
11 years...	7	1360	1	1238
12 years...	5	1416	2	1245
13 years...	8	1487	3	1256
14 years...	12	1289	5	1343
15 years...	3	1490	8	1238
16 years...	7	1435	15	1273
17 years...	15	1409	18	1237
18 years...	18	1421	21	1325
19 years...	21	1397	15	1234
20 years....	14	1445	33	1228
21 years...	29	1412	31	1320
22 years...	26	1348	16	1283
23 years...	22	1397	26	1278
24 years...	30	1424	33	1249
25 years....	25	1431	33	1224
Total.....	415		424	

When the data in Table II. are cast in the form of a curve representing the increase in weight according to age, we obtain the chart given below.

In the records of Vierordt it appears that, except at birth and in the fourteenth year, the male has a greater brain weight than the female.*

* During the period of very rapid growth, a slight disparity in the average age of the cases compared easily reverses the weight relations according to sex. This is the probable cause of greater weight in the female at "birth," as reported by Vierordt. More careful determinations by Mies, 1894, and Pfister, 1897, show the male brain to be heavier.

In both sexes the most rapid increase in weight is during the first year; it continues to be rapid up to the fourth or fifth year, and then becomes slow till the seventh year, when the weight of the brain found in the adult is nearly attained. From this age on, there is a very slight and very slow growth up to the fifteenth year. At the time when nearly the final brain weight has been attained—namely, the seventh or eighth year—the full difference of 100 grams or more existing between the two sexes is evident. From this, it is seen that the rapid growth of the brain has occurred while the body is still very immature, since boys of seven years weigh on the average only fifty pounds, and girls but forty-two pounds—this in both sexes being about one-third of the adult body weight; and that the differences characteristic of sex have been established before sexual maturity. The irregularities of the curve are to be explained as mainly statistical and dependent on the comparative smallness of the number of cases available for each year. No significance is to be attached to the dip in the male curve at fourteen years. The very high averages for the males at thirteen and fifteen years, and for the females at fourteen years are to be noted since they articulate with the findings in other series (see Pearl, 1905) which give the maximum mean weights between the ages of 15 and 25 years. These observations, therefore, appear to represent a true condition—the weight of the human brain reaching its maximum about the middle of the second decade or a few years later. Excluding the effect of the fatal illness the weight of the brain is probably nearly constant from this age up to the beginning of the sixth decade. The slight fall in weight from the maximum to the end of the curve as given in the chart is explained as the result of the fatal illness acting on a brain in which the resistance to wasting very slowly decreases. This same influence modifies the brain weight during the next thirty years of life (twenty-five to fifty-five years). From this time on a normal decrease in weight seems to occur and to this is added the increasing influence of the fatal disease. There is some probability that in the more favored social classes the shrinkage after the sixth decade occurs more slowly. From the table of final weights (Table I.) as well as from that just presented on growth, it is plain that the difference in the weight of the encephalon according to sex is one exhibited from the time of birth; that it increases during the growing period, and is maintained throughout life. This difference almost disappears, however, when the comparison is made after correction for body weight and stature (Blakeman, Lee and Pearson, 1905).



Curves Showing the Variations in Brain Weight During the First Twenty-five Years of Life. Based on Table II.

Table III.—Percentage Value of the Body Weight as Represented by the Encephalon at the Ages Named. (Based on data from Vierordt.)

Age.	Brain weight.	
	Male	Female.
Birth.....	12.29	12.81
One year.....	10.50	11.39
Five years	7.94	7.98
Ten years.....	5.59	5.56
Fifteen years.....	3.62	3.09
Twenty years....	2.43	2.31
Twenty-five years.	2.16	2.23

The relative brain weight in the two sexes is therefore nearly the same, as can be seen from Table III.

It is an important fact that the differences in the weight of the encephalon according to sex, age, and stature are correlated with only very slight variations in the proportional development of the subdivisions of the encephalon as here examined. Table IV. shows the percentage value of these subdivisions for different ages at all statures.

TABLE IV.—SHOWING THE PERCENTAGE OF WEIGHT OF THE SUBDIVISIONS OF THE ENCEPHALON, THE RECORDS BEING GROUPED ACCORDING TO AGE. BASED ON TABLE I

Males.						Females.			
Age.	Encephalon.	Cerebrum.	Cerebellum.	Stem.	Stem.	Cerebellum.	Cerebrum.	Encephalon.	Age.
20–40	100	87.52	10.49	1.91	1.96	10.9	87.13	100	20–40
41–70	100	87.00	10.6	1.94	2.02	10.8	87.14	100	41–70
71–90	100	87.33	10.6	1.98	2.11	11.16	86.40	100	71–90

Here there is a very slight falling off in the proportional value of the cerebrum in persons of advanced age. In general the value of the male cerebrum is slightly in excess. In the next table (V.), where the comparison is made according to stature, there is a regular decrease in the value of the male cerebrum with diminishing stature, and at all statures the male cerebrum is slightly in excess of the female.

TABLE V.—SHOWING THE PERCENTAGE OF WEIGHT OF THE SUBDIVISIONS OF THE ENCEPHALON, THE RECORDS BEING GROUPED ACCORDING TO STATURE. BASED ON TABLE I.

Males.						Females.			
Stature.	Encephalon.	Cerebrum.	Cerebellum.	Stem.	Stem.	Cerebellum.	Cerebrum.	Encephalon.	Stature.
175 cm. and upward.	100	87.5	10.5	1.90	1.91	10.86	86.93	100	163 cm. and upward.
172–167 cm.	100	87.2	10.65	2.08	2.10	11.16	86.68	100	160–155 cm.
164 cm. and under.	100	87.17	10.6	1.86	2.09	10.83	87.06	100	152 cm. and under.

In Table VI., it is possible to make the comparison of the proportional development of the several divisions from birth to old age.

TABLE VI.—SHOWING THE PROPORTIONAL WEIGHT OF THE DIVISIONS OF THE ENCEPHALON AT DIFFERENT AGES. (Boyd.)

Males.					Females.				
Number of cases.	Age.	Cerebrum.	Cerebellum.	Stem.	Number of cases.	Age.	Cerebrum.	Cerebellum.	Stem.
45	New-born.	92.4	5.8	1.60	45	New-born.	92.1	6.2	1.50
22	7–14	87.8	10.3	1.61	18	7–14	87.9	10.5	1.50
99	30–40	87.3	10.6	1.98	80	30–40	87.0	10.8	2.01
95	70–80	87.0	10.7	2.09	128	70–80	86.9	10.9	2.15

We see here that the cerebellum is the portion least developed at birth, and that between birth and the seven- to fourteen-year period the proportions found at maturity are very nearly established. In this table, again, the percentage value of the cerebrum tends to be slightly greater for the male. During the active growing period the reduction in the percentage value of the cerebrum is due, of course, to the more rapid growth of the cerebellum, while during the involutionary period—that is, between seventy and eighty years, in this table (VI.)—the diminution in value is due to its more rapid shrinkage, as can be seen by examining the absolute weights exhibited in Table I.

As regards the subdivisions of the cerebrum, Franceschi (1888) has some observations that are unique. He determined the weight of the thalamus and striatum for each half of the cerebrum, in a number of persons and at various ages. During the first five years, the records are too few and indefinite to be valuable. Beginning with twenty-one years, however, he has the following data to present:

TABLE VII.—GIVING THE WEIGHT OF THE BASAL GANGLIA IN THE TWO SEXES AT DIFFERENT AGES. WEIGHT IN GRAMS.

Males (Basal ganglia).				Females (Basal ganglia).			
Age.	Number of observations.	Mean weight.		Age.	Number of observations.	Mean weigth.	
		Right.	Left.			Right.	Left.
21–40	16	41.2	40.8	21–40	20	36.0	36.0
41–70	38	41.6	42.3	41–70	45	37.7	38.0
71–87	22	42.4	42.4	71–87	21	37.7	41.0

This table shows no regular difference between the two halves of the brain. There is, however, a constant difference according to sex, these structures being about ten per cent. heavier in the male. This corresponds with the percentage difference between the sexes for the entire encephalon and thus shows that the basal ganglia have the same proportional weights in both. Very curiously, an actual increase in weight occurs in the last age group, when according to the other records the total weight of the cerebrum is *less* than that found during the prime of life. This peculiar relation must be confirmed before it can be regarded as significant.

In the one instance where it has been carefully studied deformation of the skull has been found to produce surprisingly little real alteration in the growth of the encephalon. The winding of a child's head with a compressing bandage so as to elongate it in a fronto-occipital axis has been practised for generations about Toulouse in France. Ambielet (1893) studied the brains of aged persons from this locality with skulls thus deformed. Naturally the effects of this deformation are more pronounced if it has been great than if it has been moderate. However, the average weight of the encephalon was diminished by this treatment only two to three per cent. while despite the highly modified shape of the skull neither the proportional weight of the cerebrum nor the weights of its several lobes were significantly altered.

This result would agree with those recently obtained from the study of crania by Boas, which he formulates as follows: "Among skulls belonging to the same type, a breadth above the average is compensated by a height and a length below the average." This is probably only a special case representing a general tendency toward a final arrangement of cranial diameters which will result in the cranial

capacity normal for the individual. The effects of bandaging the skull appear to cause a general nutritive disturbance rather than one limited by the boundaries of the bandage, and the results are not due to direct pressure on the enclosed brain. So far as this aspect of the problem is concerned, we have the beautiful researches of von Gudden on the growth of the skull and brain, which show that while these two structures may to a slight extent mutually adapt themselves to each other, yet the fundamental growth changes in the brain are in a high degree independent of merely mechanical conditions.

2. *Spinal Cord.*—The weight of the spinal cord at different ages can be best shown by a tabulation of the results, though these are hardly numerous enough to be used for the formation of a curve (see Table VIII.).

Table VIII.—Giving the Weight of Human Spinal Cord at Different Ages.

Age.	Weight of cord in grams. Male.	Female.	No. cases.	Observer.
Birth.	3.4	.	10 males. 11 females .	Mies ('94).
1 mo.	3.9	3.8	106 males.. 104 females	Danielbekof ('85)
2–3 mos.	5.0	4.6		Pfister ('97).
4–6 mos.....	7.1	6.1		Pfister ('97).
7–10 mos.....	8.2	7.5		Pfister ('97).
11–15 mos....	10.7	10.5		Pfister ('97).
16–21 mos....	.	11.0		Pfister ('97).
2–3 yrs . .	13.0	13.6		Pfister ('97).
3 yrs. to 4 yrs. 7 mos.	15.7	14.8		Pfister ('97).
5 yrs. to 6 yrs. 5 mos.	18.9	18.2		Pfister ('97).
6 yrs.....	16.9	....		Mies ('94).
10 yrs. 9 mos.	...	17.3		Mies ('94).
18 yrs. 6 mos.	27.5	.		Mies ('94).
Maturity	27–28	.		Ziehen ('99).

It thus appears that the spinal cord increases from an average weight of 3.4 grams at birth to 27–28 grams at maturity—an increase of nearly eightfold—thus showing a gain in relative weight which is about twice that of the encephalon. The encephalon has nearly attained its adult weight at the seventh year, while the cord (see table) at this time has less than two-thirds of its adult weight. So far as this table shows, the cord grows about as rapidly as the brain during the first four years after birth at which time it has attained only a little more than one-half of its final weight. Its subsequent growth is therefore much greater than that of the brain. The final enlargement of the cord is correlated with the growth of the trunk and limbs that occurs during adolescence—a series of changes by which the cranial cavity is slightly affected. The weight of the cord is therefore correlated with the length or the capacity of the vertebral column.

B. Percentage of Water.—Touching the chemical changes which are correlated with growth we shall here present only those on the percentage of water. This character is most closely correlated with age and hence is a function of time—being largely independent of variations in the nutritional environment (Donaldson 1911).

In the growing neuraxis the changes in weight run nearly parallel to the changes in volume, but are a trifle more rapid, owing to the fact that with advancing age the specific gravity of the nerve substance increases as the percentage of water decreases. The observations which relate to this character in man appear to the brain only and are for the most part scattered and difficult to interpret, but there remains a small number which may be directly used. In Table IX. are given the percentages of water in the brain at birth and at maturity and for two intermediate ages, the data for man being compared with those for the albino rat at equivalent ages (Donaldson, 1910).

Table IX.—Table Showing the Changes in the Percentage of Water in the Brain from Birth to Maturity in Man and in the Albino Rat.

Man. Age (years).	Man. Percentage of water.	Rat. Percentage of water.	Rat. Age (days).
Birth.....	88.3	87.7	Birth.
2 years.....	81.1	81.3	26 days.
9.5 years.....	79.2	78.6	115 days.
Maturity.....	77.0	77.4	300 days.

Table IX. shows that in man and the albino rat the range in percentage of water between birth and maturity is about the same—a little more than ten points. It further shows that the period of rapid diminution in the percentage of water occurs during the period of rapid growth of the brain (approximately the first tenth of the span of life). Without going into the details of an explanation it may be noted that the data for the rat show similar relations at equivalent ages. This loss in the percentage of water is commonly regarded as the result of the medullation process. There is reason to think, however, that the two changes do not stand in causal relation but that they are merely concomitant (Donaldson, 1910). As regards the spinal cord there are no data for the percentage of water in man. In the albino rat the percentages are 85.6 per cent. at birth and 68 per cent. at maturity and the curve of loss is similar to that for the brain. It is highly probable that the human spinal cord would show similar values.

C. Growth Changes in the Neuraxis Considered as the Resultant of Changes in the Cells which Constitute it.—The changes which occur in the central nervous system as a whole are but the resultant of all the changes taking place in the cells which compose it. An exhaustive list of these components would comprise the cells forming the blood-vessels and the several sorts of supporting structures—ependyma, neuroglia, and connective tissue—in addition to the neurones proper. Lack of information concerning growth in the non-nervous structures will, however, preclude more than incidental mention of them, and we can turn our attention to the neurones, not, however, forgetting that the non-nervous structures are much more important constituents than this treatment of them would indicate.

1. *Number of Neurones.*—The cessation of cell division in the human neuraxis has been but little studied. From the observations on animals (Allen-rat), however, we may infer that in man it usually becomes very slow or stops about the time of birth or shortly after, except in the cerebellum where it may continue in the outer granule layer well into the second year of postnatal life (Berliner, 1905).

Speaking broadly we may consider that the number of cell elements is nearly complete at birth and hence not subject to material alteration by variations in the environment. These cells however exhibit at birth great differences in their degree of development, some being far advanced while others are extremely immature. During the further growth and differentiation of the immature group nutritive

conditions may have a profound influence. The development from the neuroblast to the mature form is usually associated with an increase in size, the cytoplasm growing more rapidly than the nucleus. From the cytoplasm outgrowths are developed. In the spinal cord cells the first outgrowth is usually the axone (neuraxone) while the dendrites appear later; on the other hand, in the cerebral cortex the main dendrite usually develops first and the growth of the axone follows (Paton, 1900; Hatai, 1902). As far as the gross form of the neurone is concerned elaboration of the dendrites may continue for a long time and the axone in addition to its terminals usually gives rise to side branches—the collaterals—and acquires a medullary sheath. Further differentiation consists in the formation of the Nissl substance and other inclusions in the pericaryon (*i.e.* the part of the cell about the nucleus), while fibrils (neurofibrils) are more or less developed in all portions of the cytoplasm and its outgrowths.

A simple classification of the neurones composing the central nervous system is the following based on their location.

I. *Afferent neurones* with their cell bodies in the spinal or cerebral ganglion. Only the axones of these enter the neuraxis.

II. *Central Neurones.*—All parts of these neurones are within the limits of the brain and spinal cord.

III. *Efferent Neurones.*—The cell bodies of which lie within the neuraxis but the axones pass to the periphery, and—

IV. *Peripheral neurones* no part of which is within the neuraxis.

These last are represented by the sympathetic system and the peripheral ganglia and do not concern us at the present moment. In central and efferent neurones a sheath of myeline is often formed first on the axone proper and next on the collaterals but not on the dendrites. In many cases, however, this formation does not occur. Recent studies in the analysis of the neurone call for a word of comment. Originally the terms axone and dendrite referred to structures distinguished by their appearance. Later it was seen that in general the function of the axone was to carry impulses *away* from the cell body and the function of the dendrites to carry impulses toward it. Recently this functional criterion has been rather generally applied. When this criterion is used for the branches of the neurones which constitute the ganglia of the afferent spinal and cerebral nerves it appears that according to the functional classification the cell outgrowth which passes to the periphery is a dendrite. It is, however, in about half the cases medullated and when medullated always has the structural character of a peripheral nerve fiber. In order to avoid confusion therefore when speaking of dendrites and axones it is necessary, as the foregoing shows, to keep in mind the two criteria which have been used.

The numbers of neurones in these several classes in the central nervous system of man have been estimated by various methods. In the case of the afferent neurones (1) the number of *medullated* fibers in the dorsal roots of each nerve has been counted on one side of one spinal cord (Ingbert, 1903) and found to be 653,627, giving a total of 1,307,254 on both sides. In the case of the central neurones Miss Thompson (1899) working with Hammarberg's plates (1895) has estimated the *well-characterized* neurones of the cerebral cortex as 9,283 millions. Blocq and Ozanoff (1892) have found the number of the pyramidal fibers going to the limbs and trunk in man on both sides to be 158,222. From Thompson's estimate of the neurones in the cerebral cortex the number in the entire encephalon has been computed to be at least 12,000 millions (Donaldson, 1911). As regards the efferent neurones Ingbert (1904) again using the number of *medullated* fibers in the ventral roots of one side of one spinal cord found the number to be 203,700 on one side or 407,400 on both sides. Since the foregoing determinations were made, further observations by Ranson (1911) have revealed in the peripheral nerves of man at maturity very considerable numbers of non-medullated fibers. Probably the addition of the non-medullated fibers would at least double the totals in both the ventral and the dorsal roots. As representing the medullated fibers these determinations are probably substantially correct but as indications of the total number of afferent neurones on the one hand and efferent neurones on the other, they are far too low. Similar corrections must be made in the case of the cortex. As was stated, the enumeration was based on the *well-characterized* cell bodies—and these are but a part of the nucleated elements, many of which though not well characterized are probably functional neurones, so that for this group also the estimate is probably too low. Despite these necessary corrections the data at hand serve to show the relative numbers of neurones in the different groups and to indicate the vast number of elements which enter into the constitution of the neuraxis in man.

Returning now to the statement that some neurones mature early in the life history of the individual, while there are associated with them immature cells which under favorable conditions will complete their development later, we find that in man for example, the number of developed cells in the spinal cord *increases* up to maturity, despite the fact that after birth there is probably no cell division of consequence, and the total number of *nucleated elements* is therefore approximately constant. Table X., taken from Kaiser (1891), illustrates this point.

Table X.—Showing the Number of Developed Cells in the Ventral Horn in the Cervical Enlargement of Man at Different Ages. (Kaiser.)

Age.	Number of nerve cells.
Fetus, sixteen weeks	50,500
Fetus, thirty-two weeks	118,330
New-born child	104,270
Boy, fifteen years	211,800
Male, adult	221,200

This same method of growth has been found in various portions of the central nervous system of the albino rat and is therefore probably characteristic for mammals at least. The fact that the maturing of the neurones takes place gradually and in series is a matter of much importance—for by this procedure according to which a fraction of the potential neurones in all of the several divisions of the neuraxis matures early, the first form of the central system represents a sketch or outline—functioning to be sure—but numerically weak, and later strengthened by the reenforcement of each cell group through the further development of those elements which at first are immature. It appears to be during this phase that disturbed nutritional conditions may readily act to arrest the course of growth.

(2) *Size of Neurones.*—If we assume that there are at least 12,000 million neurones in a human encephalon weighing 1,400 grams the following calculation can be made. There is reason to think that at least ninety per cent. of the encephalon is composed of neurones, these therefore weigh 1,260 grams. The specific gravity of the encephalon is about 1.037 which makes the volume of the neurones 1,215 c.c. Dividing this volume by the number of neurones we obtain as the average volume $101{,}250\mu^3$ which represents a cube a little less than 47μ on the edge. Of course many neurones have a much greater volume than this and on the other hand, a vast number are smaller.

To avoid possible misunderstanding attention is especially called to the fact that this value represents the volume of the cell body and all its branches (dendrites and axone) combined. Moreover, it must be remembered also that if the total number of neurones which we have assumed is too small, then this average volume is correspondingly too large.

The preparations of His (1889) show the neuroblast to have a volume of about $700\mu^3$ so that if we take this as the initial value then the average enlargement from neuroblast to mature neurone is about 144 fold.

Since it can be shown that many neurones increase more than a thousand times in volume it follows that there must be a very large number of neuroblasts which develop either slightly or not at all. In support of this statement, attention is called to the fact that in the cerebral cortex cell bodies of the smallest neurones have diameters much smaller than that of the original neuroblasts; while in the cerebellar cortex, the granules with a mean diameter of about 7μ appear still more reduced. There is at present no satisfactory explanation for these cases.

If for purposes of computation we take the weight of the male encephalon as 380 grams at birth and 1400 at maturity it follows that the encephalon has increased 3.7 times in weight during this interval, and the increase in volume is of course nearly the same. Thus between birth and maturity the average volume of the constituent neurones becomes only about 3.7 times what it is at birth. At birth, however, the average volume of the neurone is some thirty-nine times that of the neuroblast. Thus of the *total increase* in the neurone thirty-nine parts occur before birth and 105 parts after that event.

In order to obtain a notion of the changes which contribute to this enlargement between birth and maturity it is desirable first to note what has been observed concerning the growth of the cell body on the one hand and of the axone on the other:

(a) *Growth of the Cell Body.*—The only observations on the changes in the volumes of growing cell bodies in man are those by Kaiser (1891), made on the largest cell bodies of the ventral horns of the cervical enlargement of the spinal cord.

Table XI.—Showing the Volumes of the Largest Cell Bodies in the Ventral Horn of the Cervical Cord of Man. Based on Kaiser's records of the mean diameters.

Subject.	Age.	Proportional volume of the cell bodies $1=700\mu^3$.*	Time interval.
Fetus	Four weeks	1	
Fetus	Twenty weeks	17	
Fetus	Twenty-four weeks	31	36 weeks.
Fetus	Twenty-eight weeks	67	
Fetus	Thirty-six weeks	81	
Child at birth		124	15 years.
Boy, fifteen years		124	
Man, adult		160	15 years.

The proportional volumes given in Table XI. show that the rapid enlargement of these cell bodies occurs before birth. It gives, however, the same values for the child at birth and the youth at fifteen years, while in the mature man the size is somewhat greater. Observations on various cell groups in the neuraxis of the albino rat confirm this result, so that it is probably true in all portions of the neuraxis that cell bodies of the largest size are found in the central nervous system at birth or shortly after.† Changes in these cell bodies which have already attained nearly their full size therefore contribute but little to the enlargement of the central nervous system during postnatal growth. The number of largest cells is nevertheless increased by the subsequent growth of those cell bodies which are still immature at the time of birth or for some time after. This is indirectly shown by another table from Kaiser giving in the same locality the numbers of well-developed cell bodies according to increasing age.

* The volume $700\mu^3$, in the fetus of four weeks, is taken from His, and the figures represent multiples of that volume.

† This statement is limited to the neurones the cell bodies of which are located in the neuraxis (classes II. and III.). The cell bodies in the ganglia of the afferent nerves (class I.) appear to grow for a longer time.

Table XII.—Showing the Number of Developed Cells in the Ventral Horn in the Cervical Enlargement of Man at Different Ages. (Kaiser.)

Age.	Number of nerve cells.
Fetus, sixteen weeks	50,500
Fetus, thirty-two weeks	118,330
New-born child	104,270
Boy, fifteen years	211,800
Male, adult	221,200

It is to be seen from this table that the number of well-characterized cell bodies approximately doubles between birth and maturity. To avoid a misinterpretation of this result the statement may be repeated here that this increase is merely in the number of mature cells and does not imply the production of *new* nucleated elements during this interval.

The contribution made to the weight of the neuraxis by the growth in the cell bodies between birth and maturity is then very moderate at best, for Miss Thompson (1899), in the study previously cited on the number of well-characterized cell bodies in the cerebral cortex of the human brain found that only 1.37 per cent. of the volume of the cortex was composed of cell bodies. On the ground that in this computation there were some losses for the dendrites not included in the measurements and for small cells which were overlooked, it was estimated (Donaldson, 1899) that two per cent. is a liberal allowance for the volume of the cell bodies of the neurones in the cortex and that this would be a liberal allowance for their volume in the remaining fraction of the encephalon as well. In discussing changes in the volume of the cell body, we have been considering therefore changes which apply to only two per cent. of the total mass of the encephalon and for this reason these changes can have but little effect on its final weight.

(b) *Growth of the Axone.*—The great changes which occur in the volume of the neurone are mainly dependent on those in the axones and the chief factor there is the development of the medullary sheath. Very early in the development of the neurone its axone appears as an outgrowth, extending from the cell of origin to its place of ending, like an outgrowing root; sometimes as in the case of the granules of the cerebellum the terminals of the axone become fixed early and the cell body draws away from this point, growth occurring in the intermediate portion of the axone.

The axones are formed gradually and their extension continues for a long time. Thus there is evidence in the spinal nerve of a frog (Hardesty, 1899 and 1900) and in the callosum of the albino rat (Ranson), that the process is long continued. Regeneration (in the peripheral nerves) is but a repetition of this kind of growth after the original axone has been destroyed in part.

At birth the great majority of the axones are almost or quite complete in the sense that they have reached the neighborhood of the cell groups where they will ultimately terminate and establish physiological connections. The enlargement of the encephalon between birth and maturity being about 3.7 times and the form remaining generally similar it follows

that by the enlargement the average length of the axones is increased approximately fifty-four per cent.

Taking the weight of the encephalon at birth as 380 grams we can make the following analysis:

	Percentage value.	Weight at birth.
Cell bodies	2	7.6 gms.
Non-nervous tissue	10	38.0 gms.
Axones	88	334.4 gms.
Encephalon	100	380.0 gms.

If we now add fifty-four per cent. to the weight of the axones—arising from the increase in the length alone—other dimensions being assumed to remain the same, this increases the weight of the axones 180.6 grams. However, while this increase in the length of the axones is going on there are at least three other processes in progress all of which contribute to the increase in their weight: (1) the formation of new axones; (2) increase in the diameter of the axones and the production of collaterals; (3) medullation.

At the present time we have no data which give direct determinations of the amount of increase which is to be credited to the first and second of these processes. Together, however, they must constitute an important contribution; concerning medullation there is more information. As the studies of Flechsig 1896) and others have shown the human encephalon is only partly medullated at birth. In the cortex this process is more advanced in the projection areas than in the far more extensive association areas. At best, however, in the encephalon as a whole medullation is very incomplete. Studies on the peripheral nervous system of the rat show that at maturity the volume of the medullary sheath is approximately equal to that of the enclosed axis cylinder (Donaldson and Hoke), Dunn (1912) . There is reason to think that this relation also holds for the medullated fibers in the neuraxis (Hatai, Koch) and we shall assume this to be the relation in the subsequent computations.

If we consider two per cent. of the total weight of the mature encephalon of 1,400 grams to be represented by the cell bodies and ten per cent. by the non-nervous structures then at maturity we have the following:

	Percentage value.	Weight at maturity.
Cell bodies	2	28 gms.
Non-nervous structures	10	140 gms.
Axones	88	1,232 gms.
Encephalon	100	1,400 gms.

As has been shown the weight of the axones at birth (some being medullated) is computed to be 334.4, subsequent growth in average length being estimated at fifty-four per cent. Growth in a brain increasing from 380 to 1,400 grams would add 180.6 grams, making a total of 515.0 grams. At maturity we find the axones computed as above to weigh 1,232 grams. If the axones at birth were all unmedullated—which they are not—and they all acquired medullary sheaths having a weight (volume) equal to their own weight then the mature medullated axones would weigh (515.0×2) 1030.0 grams and this would leave only (1,232−1,030), 202 grams to cover the formation of new axones and the increase in their diameters, the latter of which changes must certainly occur during postnatal growth. It is evident therefore that despite the active medullation which occurs during postnatal growth a vast number of axones must remain unmedullated. The foregoing analysis which represents the axones of the encephalon as a residuum after abstracting the cell bodies of the neurones and the supporting tissues—while essentially correct, is admittedly crude. Not to be misleading, the picture must be rendered more precise by recalling the large fraction of the encephalon represented by the cortex of both the cerebrum and cerebellum, the reduction of the mass of white substance produced by the infolding of the cortex in gyrus formation and finally by the fact that in the cortex itself the proportion of the *medullated* fibers is relatively small. It is probable that this does not exhaust the list of compensating factors which modify the computation just given, but despite these possible corrections it remains evident that the greatest part of the changes in the weight of the encephalon is dependent on changes in the axones and in this the formation of the medullary sheaths plays a very prominent part. The suggestion lies close at hand that individual variations in the amount of medullation may be one of the most important causes of the individual differences in brain weight.

Before leaving this general topic a word should be said about the size (volume) of the neurone in the mammalian series. Several series of observations have been made. The results obtained by Hardesty ('02) are given in Table XIII. It is to be noted that in all these cases the cell bodies only have been subjected to measurement.

Table XIII.—Showing in a Series of Mammals the Mean Diameters Determined in Each Case by Measuring the Ten Largest Cells in the Ventral Horns as They Appeared in Three Consecutive Cross-sections Made Through the Cervical Enlargement of the Spinal Cord. (Hardesty.)

Animals (arranged according to normal body weight).	Average mean diameter (in μ).	Computed relative volumes (based on the mouse as standard).
Elephant (Indian)	84.4	30.0
Ox	65.0	13.7
Horse	61.9	11.6
Man	58.0	9.7
Hog	55.5	8.5
Dog	58.7	10.0
Monkey (Cynocephalus babuin)	54.0	7.8
Cat	53.5	7.6
Rabbit	39.2	3.0
Rat (albino)	34.7	2.0
Mouse (albino)	27.4	1.0
Bat	30.6	1.4

The results given in this table are in substantial agreement with those obtained by other investigators all of which show that in the *types of cells examined* the *volume* of the cell body is in general (though not always) smaller in smaller animals, but since it does not diminish nearly as fast as the body weight it becomes in reference to body weight relatively larger in the smaller forms. This, however, is a character which the nerve cells share with all the other types of cells when mammals of different sizes are thus compared. The volume of the cell bodies of the spinal ganglia is also closely related to body weight—but in the case of the other neurone groups, as for example, the Betz cells of the cerebral cortex, other influences seem to be more important and some of the smaller carnivora show Betz cells which are very large in proportion to their body weight.

The cell body is as we know, only the lesser portion of the neurone, the axone as a rule being greater in weight. When we consider the latter several relations require to be examined. No systematic study has been made as yet to determine whether in different mammals cell bodies of the same size and belonging to the same class have axones of like diameters or whether the axones decrease in diameter as we descend in the series. It is certain that as a rule they do not increase. Leaving this question, however, as unsettled, it is self- vident that in the smaller species

the average length (*i.e.* distance traversed by the axones) is less than in the larger species, hence the axones are certainly less in volume in the smaller species. We may safely say therefore that in general the smaller mammals have absolutely smaller neurones, while at the same time the relative size of the neurones increases as the animal diminishes in size. The physiological significance to be attached to the size of a neurone has still to be determined. The best we can do at present is to conclude from certain histological relationships that within a given species the larger a cell body and the greater the number of dendrites, the more opportunity do terminals from other neurones have to come in contact with it, and thus the larger the number of axones over which impulses may reach the cell. Similarly an axone of large diameter tends to split and branch in its course and to produce a large number of terminals, thus putting the cell body from which it arises into physiological connection with a large number of other neurones. These observations give us the concept of coarseness and fineness in the structure of the nervous system and also suggest several important physiological corallaries.

D. Growth Changes in the Cerebral Cortex.—Despite the interest which attaches to growth changes in the cerebral cortex our information is still very imperfect. In the albino rat the cortex on the lateral aspect of the cerebral hemispheres in a frontal section made at the level of the optic chiasma shows between birth and old age the thicknesses given in Table XIV.

Table XIV.—Albino Rat. Thickness of Cell Layer of Cortex in Millimeters. Specimens Fixed in Formaldehyde and Imbedded in Paraffin.

Weight of rat in grams.	Age.	Thickness of cell layer.
4.6....	Birth ...	.40
10.4....	Ten days	.82
25.7....	Twenty days..	1.32
68.5.....	Fifty days	1.37
159.2.....	Maturity	1.49
242.....	Old age..	1.36

In this animal therefore the cortex grows not only in area but in thickness also as the brain enlarges. In man according to Kaes ('07) the cortex does not thicken but becomes thinner from birth to maturity. The solution of this paradox lies in the fact that the measurement of thickness is made by Kaes from the ectal border of the fibræ propriæ to the ectal surface of the cortex. Since the band of association fibers represented by the fibræ propriæ increases in thickness during the first seven years after birth, without any notable thickening of the remainder of the cortex it follows that during this period the thickness of the cortex as so measured diminishes. There may be some diminution after this age, but it is slight at best.

On the other hand, when at maturity a locality is found in which the cell layers in one hemisphere have a greater thickness than in the corresponding locality of the opposite hemisphere we are justified in calling the thicker cortex the better developed. Mellus (1911) has shown that in the third frontal convolution of the left hemisphere the cortex is thicker and hence better developed than in the right side. This is the first case in which a well-marked asymmetry in the cerebral cortex has been observed. In the great sensorimotor region about the central fissure Passow (1899) has been able to show that the association fibers at maturity are developed best in the more ventral portion of the region which contains the (discharging) pyramidal cells controlling the movements of the lower arm, hand, and face. In the child at one and three-quarters years this layer is equally developed through the length of the gyri, that is, there is no differentiation between the cell groups controlling the leg and the proximal portions of the arm and those which control the distal portions of the arm, and from this we infer that the cortical control of the finer muscles and finer movements increases for some time after that for the coarser movements has been completed.

E. Neurones in Old Age.—After the middle of the fifth decade there is a marked tendency for the encephalon to diminish in weight. Concerning the spinal cord we have no observations. The percentage of water is at its lowest after the prime of life, but the loss of water thus indicated accounts for only a very small fraction of the total loss which has just been mentioned. Most of the neurones have a life conterminous with that of the individual. However, some may be destroyed in advanced age. Thus Hodge (1894) has noted a diminution in the number of the Purkinje cells in the cerebellum from a man dying at the age of ninety-two. Replacement of neurones thus lost is not known to occur.

There is scattered evidence to show that in advanced age the cell body and the nucleus shrink, nucleoli disappear and the perikaryon becomes loaded with formed materials like pigment and not valuable to the cell for nutritive purposes. Dr. Dunn (1912) has recently pointed out that in the old albino rat the peripheral nerve fibers shrink to a diameter below that found in the prime of life. Although evidence for such shrinkage, which involves both the axis and the enclosing medullary sheath, has not yet been obtained directly in the central nervous system, it is highly probable that it occurs there and is one of the chief causes of the loss of brain weight after the fifth decade. It seems further probable that not only do the individual neurones thus change toward the end of life but also that the connections between them are here and there interrupted, thus diminishing the physiological paths between the various elements.

F. Summary.—The following statements are limited to the encephalon. From birth to maturity the human encephalon increases about 3.7 times in weight. At seven years it has attained nearly its full weight and at about fourteen years reaches its maximum. This maximum is maintained until the fifth or sixth decade when there appears a slow loss in weight, which continues to the end of life. From birth on the specific gravity of the encephalon increases. This is accompanied by a continuous loss in the percentage of water. This loss being most marked during the period of most rapid increase in brain weight. The changes in the weight of the encephalon are the result of changes in the weight of its constituent elements. We credit ten per cent. of the weight to non-nervous elements and ninety per cent. to the constituent neurones. The number of neurones is estimated at 12,000 millions—probably an underestimate. At birth, cell division is nearly complete except in the cerebellum. According to the foregoing data the average increase in the volume of a neurone between birth and maturity is 3.7, while the mature neurones are on the average 144 times more voluminous than the neuroblasts giving rise to them. A very considerable number of the neurones undergo only a slight enlargement. The cell bodies of the neurones form only about two per cent. of the volume of the encephalon. The increase in the weight of the encephalon is therefore mainly due to the growth of the axones and in this growth the formation of the medullary sheath plays an important part. It is probable that at maturity the volume of the medullary sheath is equal to the volume of the axis cylinder which it surrounds.

At birth a number of the neurones have attained

approximately their mature form and these elements in different localities have in many cases established functional connections at that time. Later the various groups are increased in size by the slow maturing of elements previously immature. The encephalon thus presents at birth an outline or sketch of its mature structure and this outline is gradually completed and filled in. This latter process occurs during the period of rapid growth, and is probably modified by nutritive conditions. The growth of the neurone is accompanied by an enlargement of the cytoplasm greater than that of the nucleus, by the formation of dendrites and the development of various inclusions within the cytoplasm. This process tends to precede the growth of the axone which first extends to the final termination, then develops collaterals and its medullary sheath and later increases in diameter, sheath and axis cylinder growing in like proportion. In general the larger neurones receive by their cell bodies a greater number of terminals which bring impulses to them and are connected by their axones, which tend to produce many terminals and make connections with a larger number of other neurones. Thus large neurones tend to make more connections than small neurones. Large neurones are the basis of a coarse structure, small neurones of a fine one. The final phase of structural growth seems to involve the formation of the maximum number of connections between all the constituent neurones, a process hardly affecting gross weight but fundamental to the highest physiological efficiency. With the approach of senescence, the encephalon loses weight and the neurones become smaller. The cell bodies shrink, lose in the proportion of the living substance in them and become loaded with inclusions not useful for nutritional purposes, while the medullated axones decrease in diameter. Some few cells may die and the connections between the cells be more or less interrupted, thus producing the physiological status characteristic of old age.

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Brain, Hemorrhage into the.—See *Cerebral Hemorrhage.*

Brain, Hernia of the.—See *Cephalocele.*

Brain, Histology of the.—See under *Brain, Anatomy of the.*

Brain, Hyperemia of the.—See *Brain, Circulatory Disturbances in the.*

Brain, Inflammation of the.—See *Encephalitis.*

Brain, Inflammation of the Membranes.—See *Meningitis.*

Brain, Malformations.—See under *Teratology.*

Brain: Midbrain Diseases.—For practical purposes, diseases of the midbrain may be grouped into three fairly distinct syndromes. These are due to the involvement of the crura, the tegmentum, and the corpora quadrigemina respectively. In actual practice, one finds that lesions are rarely strictly confined within these anatomical limitations, but when more or less clearly delimited, the syndromes are fairly characteristic.

The midbrain contains all the motor and sensory pathways, as well as a number of special centers. Therefore, one expects to find marked involvement of the motor or sensory tracts in association with implication of these special centers. A longitudinal section of the brain stem shows the limitation of this midbrain area to be bounded caudad by the front edge of the pons, and cephalad by the upper border of the anterior corpora quadrigemina. The aqueduct of Sylvius penetrates its entire length in its dorsal aspect. On cross-section a division into three fairly well-marked areas is apparent; the cerebral peduncles below, divided by the substantia nigra into the crura below and the tegmentum above, and the anterior and posterior corpora quadrigemina. Still further above it contains two paired structures, the red nuclei. Its chief nuclear structures then are the anterior and posterior corpora quadrigemina, the red nuclei, the nuclei of the third and fourth nerves, the central gray nuclei, the small nuclei of the fifth nerve, the nuclei of the posterior commissure, and of the posterior longitudinal bundles, and the nuclei of the substantia nigra. On its upper border, it is in close relation with the thalamus, and the median and lateral geniculate bodies.

SYNDROME OF THE CRURA CEREBRI.—The crura consist essentially of the long motor pathways, which run on the ventral surface of the midbrain; these are chiefly the corticopontine, and the corticospinal or pyramidal tracts. This part of the midbrain, or the brain stem, is injured frequently as the result of hemorrhages or softenings, or by tumors growing within the mid-brain itself, from the skull, or from the meninges. Cerebrospinal syphilis with gummata is not an infrequent cause of the production of this syndrome of the crura cerebri. This syndrome is also known as the Weber (Guebler-Weber) or superior alternate hemiplegia syndrome. When due to hemorrhage or thrombosis the chief arteries involved are the posterior cerebral, from which a number of branches, called by Dastros the internal peduncular, are given off. These internal peduncular branches enter the internal portion of the peduncles, but

rarely pass beyond the substantia nigra. The anterior external peduncular arteries also supply the cerebral peduncles, and go as high up as the thalamus.

The Weber syndrome is a crossed paralysis, consisting of an oculomotor nerve palsy, with a spastic palsy, a hemiplegia, of the entire opposite side of the body, usually including the face. The size and the site of the lesion will determine in large part the intensity as well as the extensity of the symptoms, the more complete oculomotor palsies developing after the fibers are collected in the interpeduncular space. Involvement of the nuclei shows less complete oculomotor signs.

These patients will usually show an initial apoplectiform attack, often rendering them comatose. After a few days they recover without signs of incoherency or confabulation. On clearing up it will be found that these patients will show ptosis, with dilated pupil, external, upward or downward squint of one eye, with signs of a spastic paralysis on the opposite side, often including the face. It not infrequently happens that more than one lesion will bring about a Weber syndrome, in which case the history of the development of the eye signs in time relationship to that of the hemiplegia is of a great deal of importance.

Treatment.—In the great majority of cases the Weber syndrome, or superior alternate hemiplegia, is due to syphilis; either syphilitic arteritis, with embolism, or thrombosis, or to a gummatous meningitis at the base. Treatment is, therefore, for syphilis of the brain, for which consult the article on that subject.

Syndromes of the Tegmentum.—Here the cerebral topography becomes more complicated, and a wider symptomatology is to be expected. A greater number of centers or paths are contained within the tegmentum; furthermore, this region is more apt to be involved by small tumors, notably those of tuberculosis; glioma and hemorrhagic softenings are not infrequent. Lesions in this region may produce hemiparesis of the opposite side; especially if the involvement is deep and the fibers of the crura are implicated. Sensory involvement on the isolateral side of the body is the rule, and here one finds a not infrequent variation in that the sensibility in the face is often much more markedly affected than that in the trunk or extremities. This is largely due to the fact that the trigeminal neuron runs separate from the main tract of the fillet. When the sensibility is involved after midbrain lesions it is apt to be involved in all of its qualities. This is often very characteristic of midbrain diseases.

Hemiataxia is a very characteristic and valuable localizing sign. It usually consists of unilateral, spontaneous movements, often closely resembling those of paralysis agitans, again partaking of the nature of an intention tremor so frequently observed in multiple sclerosis. The particular type of tremor will depend largely upon the exact location of the lesion. This hemiataxia is largely due to sensory disturbances and apparently is a result of implication of the cerebrorubrothalamic fibers. It is usually homolateral to the lesion on the side opposite to the hemiparesis. If the lesion reaches out into the superior peduncles, the intention quality of the tremor increases.

In lesions in this region a special syndrome also (the Benedict syndrome, *q.v.*) has been described. It consists essentially of a third nerve palsy, with a tremor on the opposite side. This in a certain sense resembles the Weber syndrome, but a tremor takes the place of the hemiparesis. This unilateral tremor partakes of the nature of paralysis agitans. Its rate is about three to five oscillations a second. It is uncontrollable, and very frequently has an intention quality; not infrequently the tremor may be partially choreiform, or partially athetoid. The trend of the tremor will depend upon the location of the lesion, and although it cannot be said that the exact mechanism has been thoroughly worked out, enough evidence is at hand to show that any involvement either of the superior cerebellar peduncle, the red nucleus, or the rubrospinal tract will induce tremors of this nature, independent of any lesion whatever of the pyramidal tract, which latter, according to the belief of Charcot, was invariably involved. Therefore, if the superior cerebellar peduncles are affected before their decussation, the tremor is usually on the side of the lesion and of the athetoid type. If the lesion lies above the decussation, or involves the red nucleus itself, it is on the opposite side, and is of the choreiform or paralysis agitans variety. If the rubrospinal tract is involved after the decussation the tremor again becomes homolateral. It cannot be said as yet that one can be too positive as to the correlations between localization and the quality of the tremor. This is one of the most interesting fields for research in lesions of midbrain structures. Hypertonicity of the muscles is a frequent sign. We therefore find that lesions of this region not infrequently bring about a syndrome closely resembling paralysis agitans, with hypertonicity and mask-like features.

The ophthalmoplegias are also common focal signs of midbrain lesions. The third nerve is most frequently involved, and gives rise to ptosis with various forms of strabismus. Lesions of the tegmentum proper rarely include the intrinsic ocular muscles. If the lesion lies pretty well back, the superior oblique may be paralyzed. Conjugate palsies are not infrequent in lesions of this region. Most frequent of these is that of loss of the upward movement of both eyes. Lateral movement conjugate palsies occasionally occur, from interruption of the pathways of the posterior longitudinal bundle.

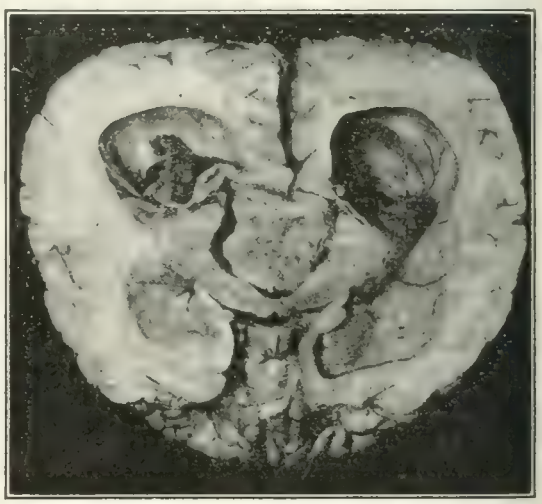


Fig. 1030.—Tumor of the Pineal Gland Pressing upon the Corpora Quadrigemina, causing the pineal syndrome.

Pseudobulbar palsy may also take place from lesions of the tegmentum. This is rarely complete, and is in large part due to the involvement of the pyramidal fibers in the tegmentum near the raphe. Here the facial muscles become weak, there is spasticity and a tendency to excessive emotional display. Swallowing is difficult, the tongue being weak, and spasticity produces indistinct or even dysarthric speech.

Syphilis is also an important factor in diseases in this region, and a Wassermann reaction should be taken in all cases showing these symptoms.

Rarely one finds in anterior poliomyelitis the occurrence of these rarer midbrain lesions. Certain of the early forms of non-progressive, so-called paralysis agitans, for instance, are in reality forms of poliomyelitis which have left premanent lesions in the midbrain.

Corpora Quadrigeminal Syndromes.—Lesions of the corpora quadrigemina bring about a syndrome often called Nothnagel's syndrome. Here the most characteristic pathological agents are tumors, either of the corpora quadrigemina themselves, or of the pineal body. When the roof of the midbrain is involved, there is usually headache and vomiting from increased intracerebral pressure. Optic neuritis often develops. Dizziness, staggering, and rolling gait, with irregular forms of oculomotor palsy are present. The conjugate vertical movements of the eyes are frequently involved, and not infrequently there is nystagmus. The pupils are usually widely dilated, or show anomalous reactions to light and accommodation. Hearing is modified if the posterior quadrageminal bodies are involved. Tumors of the pineal body (See *Pineal Syndrome*) offer special features for consideration. These have been studied particularly by Bailey and Jelliffe, and consist of (1) general symptoms of intracerebral pressure, (2) oculomotor palsies with disturbed pupillary reactions and other signs of involvement of the corpora quadrigemina, and (3) metabolic symptoms, due either to the disturbed pineal itself, or to infundibular hydrops and pressure upon the pituitary. The metabolic symptoms are interesting, often consisting of adiposity, sexual precocity, with premature development of the sexual characteristics, and occasionally cachexia. Lesions anterior to the midbrain involving the thalamus give a special symptomatology which will be discussed in a later volume under the head of *Thalamic Syndrome.* Smith Ely Jelliffe.

Brain, Physiology of the.—Functions of the Brain.—A relation between the brain and mental processes, sensations, and the production of voluntary movements, has been believed, at various times, for centuries. Scientific acceptance of a relationship between the brain as a whole, or its parts, and certain mental processes is, however, quite recent. Disregarding philosophical speculation, which may lead, and which often does lead, to inconclusive judgments, we may admit that there is a definite relation between the activities of the brain and those activities which are called mental phenomena, or which are very generally grouped together under the general term "mind." Speaking in terms which are not scientifically exact we often say that the brain is the "seat of the mind." From time to time many views have been put forth disputing this relation, and there have been advocates of the localization of particular mental processes in other special parts of the nervous system and even in other parts of the body. The guesses of the ancients regarding this matter have been paralleled in recent years and it is sufficient to note that there have been advocates of the localization of special mental processes in parts of the cerebellum, in the midbrain, and even in the muscles of the body.

The Principle of Cerebral Localization.—Although in some quarters it is tacitly assumed that the principle of cerebral localization has been settled, the question is periodically discussed and an examination of the literature makes it apparent that the term localization is used in widely different senses. To obviate circumlocution in the description of mental-cerebral relations expressions are often used which, a careful analysis shows, are not entirely warranted by the facts, and which very often lead others, if not the writer, to draw absurd conclusions and illegitimate theoretical interpretations. Because of this, it is important that the meaning of the term localization be considered.

That the cortex may be divided into a number of areas which have special histological characteristics is a well-established fact. That some of these areas are known to be associated in a general way with certain motor and sensory processes is also admitted, since it is recognized that destructions of special areas are accompanied by defects of movement and of sensation. It not has been established, however, that the mental (sensory, etc.) changes accompanying cortical destructions differ from those accompanying subcortical destructions. The best evidence that has been found for the association of particular mental processes with separate parts of the brain is that obtained from the study of aphasic patients, but the facts do not warrant the conclusions. What is observed in these patients are losses of the ability to articulate, or to understand, but many clinicians suppose additional psychic alterations, *e.g.* in motor aphasia, the loss of motor images of articulation, the loss of kinesthetic memories, etc. These suppositions have been accurately characterized by Morton Prince as metaphysical psychology, for they are gratuitous assumptions without a basis in fact.

It would take too much space to deal with other similar suppositions which have been made the basis of broad generalizations regarding mental and cerebral relations, but although facts are wanting to enable us to conclude that special parts of the brain are used for special mental states, convenience demands the use of terms which critically may be believed to contain this conclusion. The reader is, however, warned not to understand the expressions as interpretations of mental experiences, but solely as convenient methods of stating certain clinical facts.

Historical.—We owe to Gall and Spurzheim the greatest impetus which was given to the study of the functions of the brain. Apart from the vagaries of phrenology, there was accumulated by Gall a mass of information regarding the structure of the nervous system, and certain functional observations on man and animals which are of great value. In their attempt at the localization of mental processes in the cerebrum, the attitude of the founders of physiognomy and phrenology was not very different from that of many to-day, for they averred "there are as many different systems (in the brain and other parts of the central nervous system) as there are different functions." Following Gall and Spurzheim, there was much discussion, and the actual localization of different functions in parts of the cerebrum was disputed by the most eminent physiologists and clinicians. Flourens, in the interpretation of his own numerous experiments and because of the results of other investigators, asserted that the cerebrum acted as a whole in all mental operation, that there was no special cerebral location for a particular mental function, and that under certain conditions even small parts of the brain could function for the whole. It was not until many facts had been accumulated through the work of a number of French clinicians, especially Lallemand, Parchappe, and Bouillaud, that the evidence became more conclusive that parts of the brain could act independently, or apparently partly so, of other parts. Lallemand and Bouillaud found that paralysis, the inability to move muscles voluntarily, was sometimes accompanied by destruction of the cerebrum, and they concluded that the part which was destroyed was that commonly used in the production of voluntary movement. Lallemand furthermore observed the fact that the destruction of one part, or of limited parts of the cerebrum produced paralysis or anesthesia, and because of the rather general association of paralysis with anesthesia he was led to conclude that "the sensations are perceived by the same portions of the brain that provoke muscular contractions, because in their cerebral

affections the same parts are deprived of movement and feeling." This view corresponds rather closely with the view expressed in more recent times, that, surrounding the central fissure, there is a sensorimotor area for the control of the body muscles, a view which has now lost most of its adherents. The startling announcement by Broca in 1861 that special lesions in the brain produced disturbances of speech, without affecting sensation and movement, was the greatest single contribution to the definite doctrine of the localization of special functions in special parts. Although we now know the observations of Broca were not exact, they were sufficiently well confirmed in subsequent years to warrant their general acceptance.

A decade later came the classical account by Fritsch and Hitzig of the results accompanying the stimulation of parts of the cortex in the brain of a dog. In 1820, Rolando had found that when the wires from a voltaic cell were connected with parts of the brain, both in birds and mammals, movements were produced, and the contractions resulting from these stimulations were found by him to be more violent, or greater, when the cerebellum was stimulated. Other investigators were apparently unable to obtain results similar to those of Rolando, and it was not until fifty years later that the results of the stimulation of the cerebral cortex were widely accepted as facts. In the meantime, however, Meynert by his anatomical work had indicated plainly that there was great probability that the anterior portion of the brain was connected with the function of movement, and the posterior portion with sensory functions.

It was mainly due to the first publications of Broca and of Fritsch and Hitzig that the attention of clinicians and physiologists was again directed to the brain, and to these early investigations there have been added during the past half century numerous observations which are important for the understanding of brain function. Since these observations have been made on both animals and man, it is important for a proper appreciation of the value of the results to become acquainted with the methods of investigation.

General Physiology.—*Methods of Investigation.*—In general our most valued method is that of combining the clinical observations of patients following accidents to or disease of different parts of the nervous system, and the examination of the brain following death. Careful observations of this character are most important since because of the function of speech more direct information of the presence or absence of perceptions and other mental states may be obtained than in animals. It is also possible to determine the capacity for voluntary movements, regarding which in animals information may be obtained only indirectly. Since, however, accidental destructions and degenerations of parts due to circulatory disturbances usually include two or more areas which the histologists show to be different in structure, there is a debit against the advantage, in that few cases have been observed in which the lesion is sufficiently well circumscribed, and it is, therefore, impossible to correlate individual functions with the physiological activity of one area.

For the understanding of the brain of man, which is the most complex of nervous structures, investigations have been made of the simpler nervous systems in animals. These investigations have been of great value, for we may produce well-limited injuries or destructions of special parts, and we may then observe the phenomena accompanying these experimental procedures. We are then enabled to acquire information regarding certain points which could not be obtained for many years should we wait for similar conditions to occur in the human brain. In the hands of the earlier investigators this method was not successful, on account of the failure to take the modern precautions of aseptic surgery, but in recent years infection of operated parts in animals has been prevented and the spread of inflammation to surrounding areas is now uncommon. One great disadvantage in animal experimentation is the comparative simplicity of cerebral structure as compared with the complexity of structure in the human organism. Another disadvantage is that the lack of the speech function prevents the acquirement of direct knowledge regarding such conditions as hypoesthesia or hyperesthesia, and regarding the mental states which an animal may have. This information may be obtained only indirectly by observing their actions. A method which was instituted by Franz in 1902 helps to obviate this difficulty. This consists in the careful observation and training of the animal previous to the operation, and the comparison of its activities before and after the experimental extirpations. It is known that animals may be taught sensorimotor habits, and it has been shown that these have been lost after the extirpations of certain parts of the brain. If appropriate selections of the sensory and motor elements of the habits are made it becomes possible to investigate the sensory, motor, and associational functions of the brain, and results may be obtained which are less open to question than the general observations which earlier investigators made, and which often led to violent controversies, such as that between Goltz and Munk.

In addition to the method of extirpation, the method of stimulation is most valuable, and only by the combination of results obtained by both methods is it possible to interpret function properly. For the investigation of the relation of the brain to the muscles, however, the method of electrical stimulation gives finer results than that of extirpation. Many years ago investigators attempted to stimulate the cerebral cortex in animals, but failed to find any reaction following the application of such stimuli. Rolando discovered that the electrical stimulation of the cerebrum, and especially of the cerebellum, was accompanied by movements of different parts, and because the movements from cerebellar stimulation were more violent, concluded that the cerebellum was the place of origin of the impulses resulting in movement. It remained, however, for Fritsch and Hitzig to demonstrate the value of this method in relation to the cerebral cortex, and this discovery was probably due partly to the fact that they stimulated the anterior part of the brain, while many previous investigators who disputed the electrical excitability of that organ, stimulated the posterior portions. Since the discovery of the electrical excitability of the brain, numerous experiments have been made on many animals, and those on the monkeys and higher apes are of very great value. In addition, in surgical operations on man in which parts of the skull have been removed, opportunities have been taken to stimulate different parts of the cerebral cortex, and to note the movements accompanying this stimulation.

Stimulation of parts of the brain other than the so-called motor cortex, although sometimes producing movement, has given very little information regarding the functions of these other parts. We have, however, a few observations on man, giving the results of stimulation of parts of the brain other than the motor regions, and the facts which have been obtained are of very great importance.

A few investigations have been made in which the effects of distant stimuli upon the electromotive state of the cerebrum have been determined. Gotch, for example, found an electric variation in the occipital lobes when the eyes were stimulated by light, but this method is so delicate and the results affected by so many external influences that it has not been extensively employed. It has probably not added to our knowledge of cerebral connection, although it would appear capable of development and of future value.

Joined with the method of observation of the activities of a man or of an animal following destruction of certain areas is that of the investigation by microscopical methods of the parts which have been affected. It has been shown that following the destruction of a part of the brain, however circumscribed this may be, degeneration of other parts takes place. Thus the destruction of the precentral cortex is known to be associated with or to be followed by degeneration of certain fibers in the corona radiata, the internal capsule and the spinal cord. This method of histopathology enables us to trace those parts of the nervous system which are closely connected anatomically, and from the observations we may deduce conclusions regarding the functions of those parts.

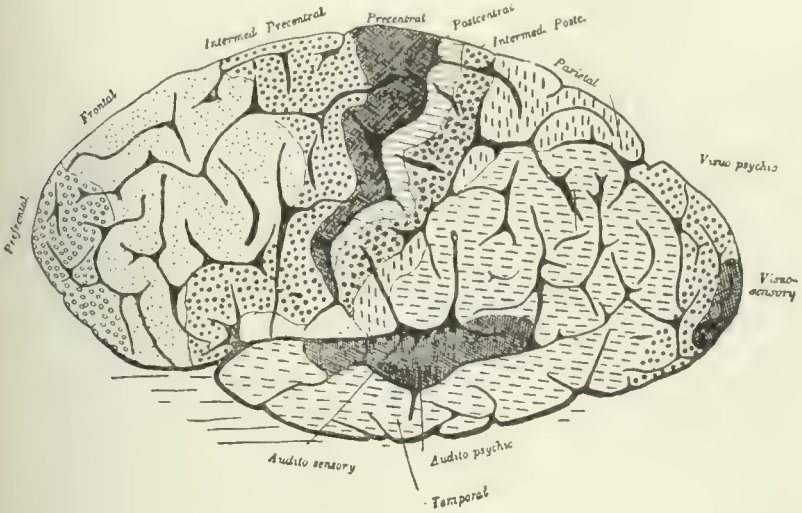


Fig. 1031.—Histological (Cytoarchitectonic and Myeloarchitectonic) Differentiation of Cortical Areas on the Convexity of the Human Cerebrum. (After Campbell.)

Examinations of the brains of embryos and young children have also been utilized for the solution of certain problems (myelogenetic method). Flechsig was able to show that parts of the cerebrum reached their complete development at different times, and with these periods of development he associated certain physiological phenomena, such as those of the control of movement and the development of sensation ability.

More recently the careful histological studies of adult brains have given us information regarding the differences of parts which from macroscopical appearances had been believed to be similar. Kaes, Ramón y Cajal, Campbell, Brodmann, Bolton, and others have found that parts of the brain which have a similar appearance to the unaided eye have certain histological characteristics which make it possible to differentiate about fifty different types of structural arrangement of cells and fibers. (Figs. 1031–1034). The older anatomists, it will be remembered, divided the cortex of the brain into a number of different parts, which were separated by fissures, but because of the recent histological studies these divisions are now recognized to be artificial and inexact. Because of the differences and the similarities in the arrangement of cells (cytoarchitectonic) and of fibers (myeloarchitectonic) there have been assumptions of differences and similarities of function which have little warrant. The use of this method in association with the clinical observations of animals and man and with the determination of the paths of degeneration does, however, bid fair to bring about a much more intimate knowledge of cerebral function. Although the location of the fields which have been differentiated by the myelogenetic method and by the myelo- and cytoarchitechtonic method differ, there are striking similarities and sufficient correspondence to warrant belief in their mutual importance.

Irritability of the Cerebral Cells and Fibers.—There has been much discussion whether or not the effects produced by electrical, chemical, and mechanical stimuli are due to the action of these agents upon the cortical cells or upon the fibers. Some have disputed the direct excitability of the cells and have contended that the fibers coming from the cells are alone affected whenever experimental stimulation is resorted to. On account of the close association of cells and fibers in the cortex, there being both cortical cells and cortical fibers, and because of the impossibility of dissociating these two elements, the matter is probably beyond definite experimental determination. There are, however, sufficient facts to warrant the belief in the stimulability of the cells when the cortex is stimulated directly by induction shocks. It is found that the strength of stimulant necessary to produce a motor response is less than that when the subadjacent fibers are stimulated. This is to be interpreted probably as evidence of a greater irritability of the cells. However, when the same strength of stimulus is used for both fibers and cells, the latent period following

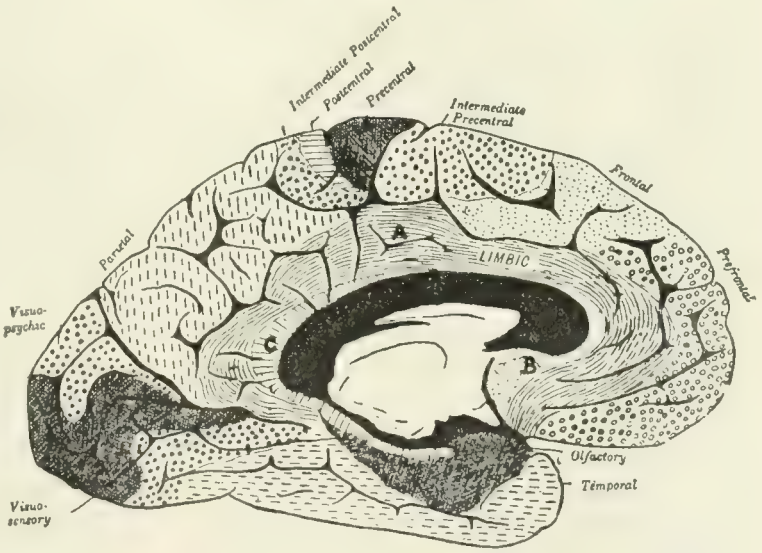


Fig. 1032.—Histological (Cytoarchitectonic and Myeloarchitectonic) Differentiation of Cortical Areas on the Mesial Surface of the Human Cerebrum. (After Campbell.)

cortical stimulation is longer than when the fibers are stimulated directly. (Fig. 1036.) This indicates that in the stimulation of the cells a certain amount of time has been consumed in the transfer or the conduction of the impulse to the fibers and the induction of the nervous impulse in the cells.

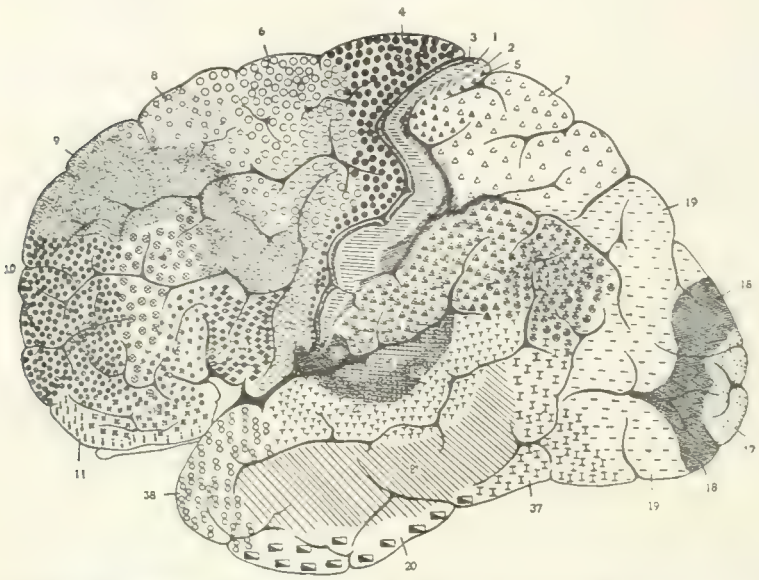


Fig. 1033.—Histological Cytoarchitectonic and Myeloarchitectonic Differentiation of Cortical Areas on the Convexity of the Human Brain. (After Brodmann.)

Although the motor fibers have an irritability less than that of the overlying cortex, the irritability of these fibers apparently increases as they pass downward as the corona radiata to make the internal capsule. At the latter place the irritability of the motor fibers approaches that of the cortical cells; but in the stimulation of these fibers, it should be noted, the resultant movements are much more diffuse than those obtained by the stimulation of corresponding cortical areas.

Numerous experiments have shown that the excitability of the cortex varies according to a number of attending conditions. When the blood supply is shut off by having the two vertebral and the two carotid arteries ligated, the brain soon becomes insensitive to stimulation. For about a minute after the stoppage of the blood supply, it is possible to obtain muscular reactions upon the stimulation of appropriate regions of the cortex, but although at first the movements are certain and of a good force, they soon become uncertain and weak, and finally no response is obtained. In this case the loss of irritability has been explained as the effect of lack of oxygen, rather than the stoppage of food supply or an accumulation of waste products, for the same result may be obtained after the ligation of the trachea. Strychnine, which has a marked effect upon the cells in the spinal cord, probably does not produce any lowering of the stimulus threshold of the brain, although because of its action on the cells intercalated or interposed between the cerebral motor cells and the muscles, it does produce a greatly increased movement. Absinthe, in spite of its general convulsive action always diminishes the cerebral excitability. In small doses alcohol and caffeine slightly increase the excitability, but larger doses of these poisons, and also chloral, chloroform, ether, morphine, and potassium bromide, reduce the irritability of the cerebral cells. Inflammatory conditions of the brain, on the other hand, heighten its excitability.

The summation effect of stimuli, a condition best known in relation to muscles, is also found when the cortex is properly stimulated. If single induction shocks, each of an intensity less than that which produces a motor response, are applied to the motor cortex at intervals of about thirty seconds a slight reaction is obtained after a few stimuli, and if the stimuli are continued, the reactions increase in intensity. Following this kind of stimulation the muscles return to their normal condition, sometimes, however, only after passing through a stage of clonic epileptiform movements. This phenomenon is of special interest because of its relation to the hypothesis of the genesis of cortical epilepsy.

When supraliminal stimuli are applied to the motor cortex at a slow rate, let us say one per second, each stimulus is accompanied by its own motor response, which has the nature of a small contraction. When the stimuli are rapidly repeated, the innervated muscles respond with a tetaniform contraction, which may be more or less complete according to the rapidity of the repeated shocks. If the stimuli are very rapid, one hundred or more per second, the muscles respond —as shown by the contraction curves, by the muscle tone, and by the electrical variations—by contractions corresponding to a rate of stimulation from ten to fourteen per second. The more rapid stimulations to the cortex, and equally so to the fibers of the corona radiata, are apparently transformed either in the

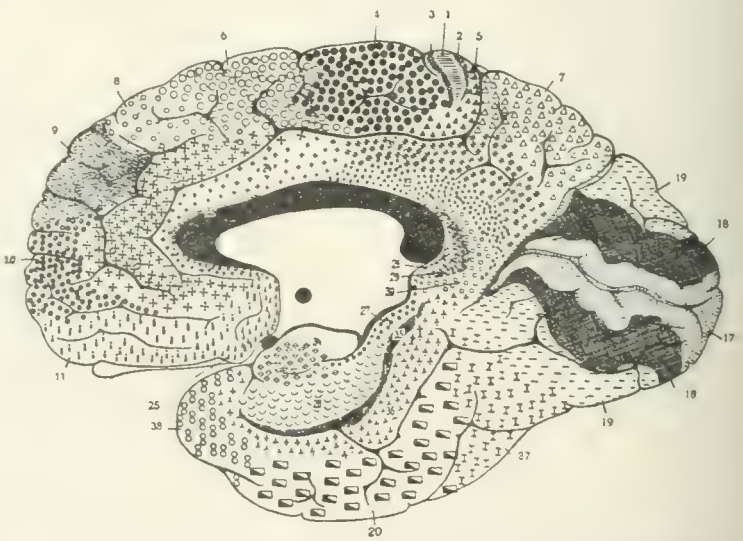


Fig. 1034.—Histological (Cytoarchitectonic and Myeloarchitectonic) Differentiation of Cortical Areas on the Mesial Aspect of the Human Brain. (After Brodmann.)

cortical cells, or in those of the spinal cord to the lower rate. A similar transformation from the continued stimulation of a mechanical character has been observed; and this fact also is interesting in relation to the production of epileptiform convulsions by pressure upon the cortex.

Some investigators have doubted the possibility of stimulation of the brain by mechanical means, but sufficient facts have been gathered to warrant the

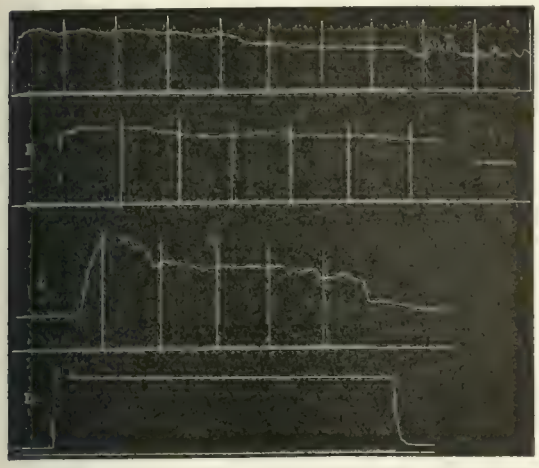


Fig. 1035.—Tracings of the Contractions of the Same Muscle of a Dog following Stimulation of Different Parts of the Motor Tract. (From Schäfer.) *A*, Leg center in the cerebral cortex; *B*, corona radiata after the removal of the motor cortex; *C*, cut spinal cord; *D*, cut motor nerve. The small lines at the base of each curve show the stimulations; the longer vertical lines, periods of seconds. Note the immediate stoppage of the contraction after the cessation of the stimulation of the cut nerve, and the gradual increased after-effect as the stimulation is given to the higher centers until the cortex is reached, where the cessation of the stimulus is followed by epileptiform movements. All curves are to be read from left to right.

belief. Often in animals during almost complete narcosis, the experimental separation by a knife cut of one part of the brain from the remainder, results in movements. This effect may not be due entirely or primarily to the mechanical effect of the section, but may also be due to the resultant hemorrhage with its mechanical and possible chemical effect. The cortical epilepsy produced by neoplasms, hemorrhages, cysts, etc., also shows that the brain may be stimulated by such mechanical means as constant pressures. Strychnine, although it does not alter to any great extent the electrical excitability of the brain, increases the irritability to mechanical stimuli. To such an extent does this poison affect the irritability, that after its absorption slight touches to the cortex may result in convulsions. A similar increase in cortical irritability to mechanical stimuli has been found in inflammatory conditions of the brain and its membranes.

Latent Period.—An appreciable amount of time exists between the stimulation of the cortex and that of the motor regions. The average time between the stimulation and the resultant movement is about 0.04 second; the variations being from 0.02 to 0.075 second. Richet has estimated that 0.02 second are taken up in the transmission of the impulse from the point of stimulation to the muscles, and in the refractory period of the latter. This would leave about 0.02 second as the period of time necessary for the action of the stimulus upon the nerve cells, and for the production of the nervous impulse.

The latent period varies for different parts of the brain and under different conditions, and some of the variations which have been noted above may have been due to differences in the amount of anesthesia, and others to differences in the location of the stimuli. Schäfer has found that the latent period for movements of the eyes resulting from occipital (visual) stimulation is about seventy-five per cent. longer than that for the movement resulting from the stimulation of the precentral (motor) cortex, and that a similar difference in time is to be noted in a comparison of the latent periods following the stimulation of the temporal and the precentral areas. It may be concluded therefore, that although movements may be produced by the stimulation of cells other than those in the precentral region, a connection between the muscles and the other cortical areas is not as direct as between these muscles and the cortex anterior to the fissure of Rolando.

Temperature of the Brain.—Many attempts were made to measure the temperature of the brain indirectly by applying thermometers to the outside of the skull, but the results of these experiments are open to so much criticism that they cannot be considered in any strict account of the temperature changes in the nervous system. Schiff was probably the first to investigate the subject carefully by applying thermoelectric elements to the brain itself, and thus was able to measure much slighter variations in temperature than had previous investigators, but he did not measure the absolute temperature of that organ. Mosso and others applied thermometers directly to the brain of animals and man, and found the temperature higher than that in the rectum. They also found, as had Schiff, that changes in nervous activity were accompanied by variations in the temperature of the brain. Great mental activity was found by Mosso to be accompanied by an increase of 0.2° to 0.3° C. in cerebral temperature, but Hill and Nabarro have shown that during active cerebral states, such as those accompanying an epileptic convulsion, there is no appreciable change in nervous metabolism. It is likely, therefore, that although the changes in temperature are easily determinable, these changes are due to something other than the oxidation of cerebral tissue, and that there is no great amount of heat produced in or by the nerve tissues during mental activity. The variations in blood supply which accompany cerebral activity are sufficient to explain the temperature changes, and these are probably the determining factors. By most careful experiments on nerves, Helmholtz and others were unable to find any changes in temperature, and it may be concluded that the results of all experiments indicate that nervous activity in itself does not appreciably alter the temperature of the brain or other parts of the nervous system.

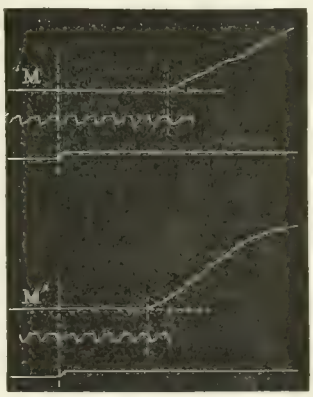


Fig. 1036.—Latent Periods of Movement Following Excitation of (*M*) Cerebral Cortex, and of (*M'*) Subjacent Corona Radiata in the Dog. In each set of curves upper line gives movement, middle line time intervals in 0.01 second, and the lower line the time of stimulation. (From Schäfer, after François-Franck and Pitres.)

Chemistry of the Brain.—Although the chemical analysis of brain tissue has not furnished any information regarding cerebral function, the facts are of interest, and possibly will have greater importance when this topic is more frequently made the subject

of investigations by physiological chemists. The most important investigations have been those of Thudicum, who differentiated numerous complex substances, of most of which the exact compositions are still open to question.

The watery content of the brain is large, that of the whole being about seventy-six per cent., of the cortex about eighty-three per cent., and of the white matter about seventy per cent. (Koch). In the young child more water is found, being about eighty-eight per cent. of the whole brain. Other differences in the composition of the gray and white substances are found as is indicated in the following table of Koch's analysis of an adult brain which weighed 1,670 grains.

	Proteins.	Extractives.	Ash.	Lecithins and cephalins.	Cerebrins.	Lipoids.	Cholesterin.
Gray substance.	47.1	9.5	5.9	23.7	8.8	0.1	4.9
White substance.	27.1	3.9	2.4	31.0	16.6	0.5	18.5

Unlike other tissues, *e.g.* muscle, the chemical reaction of the brain does not change to acid during activity, but this may be due to the slight amount of chemical change which takes place. The acid reaction is found after death and is said to be particularly rapidly produced in the gray matter.

Movement.—The fact that injuries to the brain were accompanied by paralyses was one of the earliest facts which indicated a relation between the cerebrum and voluntary movement. The definite relation of the cerebral cortex to the production of

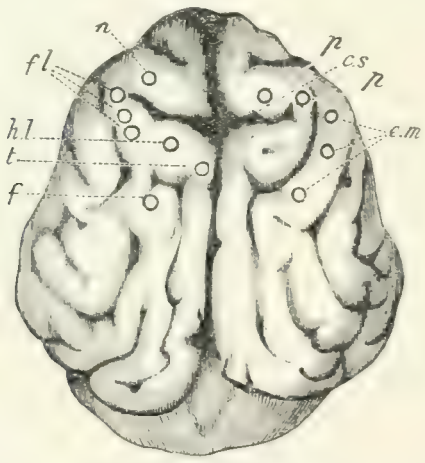


Fig. 1037.—Cortical Motor Areas of the Dog's Brain. (From Stewart, after Hitzig.) *n*, Neck; *f.l.*, forelimb; *h.l.*, hindlimb; *t*, tail; *f*, face; *p*, dilation of pupil, especially of opposite eye; *e.m.*, eye movements; *c.s.*, crucial sulcus, believed to be the homologue of the central fissure in man and higher animals. Motor areas indicated unilaterally; there are corresponding areas in both hemispheres.

movement may be said to have been recognized when the stimulability of this part was established by the work of Fritsch and Hitzig. It was found that upon stimulation of the anterior portion of the dog's brain, movements of the neck and forelimbs were obtained. These positive results led to extensive investigation of the excitable areas in animal brains, and to the more careful clinical and pathological examination of patients. It is upon the combination of the results of their studies that our present conceptions are founded.

Although the early experimenters obtained movements upon stimulation of a large part of the cerebral cortex, subsequent experiments have shown that the movements in man, in monkeys, and in the higher apes are obtained only upon stimulation of the cortex anterior to the fissure of Rolando. The results of the experiments of Grünbaum and Sherrington have demonstrated that the excitable motor area for movements of the body lies entirely within and anterior to the fissure of Rolando, and, furthermore, they demonstrate that the movements are not movements of single muscles, but movements of parts. They distinguished, as had not been done previously, between muscular contraction and movement; and they showed that upon the stimulation of the cortex single muscles were not activated, but that groups of muscles were made to function in such a way that definite movements of apparent usefulness were obtained. From their experiments on this point, and this has also been confirmed by the investigations of the Vogts, it must be concluded that there is no representation in the cerebral cortex for the contraction of individual muscles; but that there is only a representation for movements. These results obtained on the higher apes have been confirmed by observations on the brain of man, when the brain has been exposed at the times of operation for the relief of cerebral affections.

By all these recent experiments on the higher apes and on man it has been demonstrated that the movements resulting from the stimulation of the cortex anterior to the central fissure are represented in areas which may experimentally be separated. Thus, at the upper portion of this area, stimulation produces various movements of the legs in man, or of the hindlimbs and the tail in animals. Below we find the cortical areas for the control of movements of the trunk muscles, next in order the areas concerned chiefly with movements in which the arm and hand are concerned, and at the lowermost point of the fissure, we find an area governing movements of the head and neck. The results of these experiments are shown in the accompanying figures, which give a more accurate account of the results than can be given by a description.

It has also been found possible to make more definite localizations than those which have been before mentioned, and in the so-called arm area, we find certain movements of the shoulder produced by the stimulation of the part of this area next to the trunk area; farther down, stimulation produces movements about the elbow and of the wrist, and stimulation of the lowermost portion of this area is accompanied by movements of the hand and fingers. Stimulation of other parts of the cortex in the frontal lobe in the higher apes produces other movements. Although movements of the head and face are produced by the stimulation of the precentral cortex, movements of the eyes are not commonly produced by stimulation of the cortex in this region. In a region which is apparently surrounded by a non-excitable zone, Sherrington discovered an area, the stimulation of which produced movements of the eyes, apparently of a more complex nature than those which are obtained upon stimulation of the precentral cortex. The movements of the eyes obtained upon stimulation of this anterior region of the brain are composed of associated movements, similar to those which are obtained in intact animals and man whenever the attention of the animal or man is directed to some particular external stimulus, and it is partly because of the similarities in reactions that some have believed the frontal lobes are concerned with the hypothetical function of attention. In this connection it is interesting to note that Ferrier observed that extirpations of the frontal lobes were accompanied by transient disturbances of

the ability to move the eyes and head in lateral directions, and that in stimulation experiments upon the frontal cortex Langelaan and Beyerman found certain disturbances in the rhythm of the heart and of

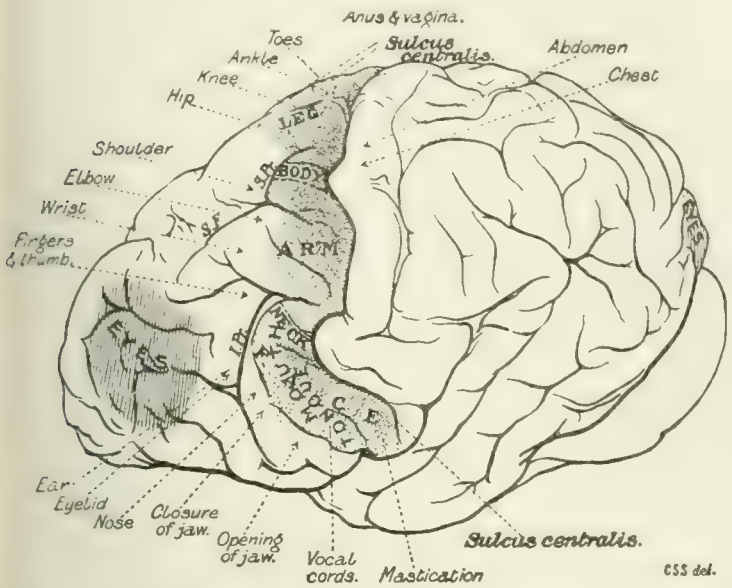


Fig. 1038.—Cortical Motor Areas on Convexity of Brain of Chimpanzee. (Grünbaum and Sherrington.) The stippling indicates the extent of the motor areas, the words indicate the parts and types of movements produced by stimulation. The frontal and occipital regions, marked with vertical lines and designated EYES, gave complex associated movements to these parts (see text for discussion).

the respiratory movements, which have also been explained by them as indications of an attention function for this part of the cerebrum. Other investigators have noted other important results following the stimulation of the motor region, that of greatest interest being the production of epileptiform convulsions.

Cortical Epilepsy.—When a point on the cortex of the motor area is stimulated electrically, the stimulation is accompanied by a movement which, from the standpoint of muscular contraction, is tonic in character. After the stimulation has ceased there is a tendency for the muscles to relax, but often there follow clonic movements of the same muscles. The general character of the movements accompanying and following stimulation of the motor area is well shown in the illustration (Fig. 1040). While it will be noted that the period of excitation is accompanied by a tonic, or long continued and steady, contraction which tends to disappear after the cessation of the stimulus, there is not an immediate relaxation, but the movement continues in the form of clonic jerks like those in epilepsy. A similar phenomenon has been observed to accompany the stimulation of the corona radiata, but only when the motor cortex is intact, or nearly so. When the cortex has been completely extirpated, the stimulation of the underlying fibers produces a tonic contraction during the period of stimulation, but this tonic contraction is not followed by clonic movements. The great difference between the movements from cortical and fiber stimulations is apparent when one compares the curves in the accompanying figures.

It has been asserted that these epileptiform movements cannot be produced by the stimulation of cortical regions other than those of the motor area, although some experimenters have found convulsions to follow strong stimulation of other parts. If, however, the motor cortex be completely destroyed, epileptiform convulsions do not accompany stimulation of other cortical areas. It appears probable therefore, that the production of epilepsy by cortical excitation of regions other than the precentral cortex is due to the diffusion or to the transfer by association of the electrical stimulation to the latter area.

In this connection the experiments of Hitzig, later confirmed by others, are of much interest. Hitzig noted, that, although the stimulation of one side of the cerebrum is normally followed by movements of the contralateral side, when the stimuli are intense these contralateral movements are accompanied by movements of the homolateral side of the body. The relation of these facts to the motor phenomena of Jacksonian epilepsy is apparent.

Paralyses.—Not only does the stimulation of the precentral cortex produce movements, but the destruction of the cells in this region is accompanied by a lack of ability to make voluntary movements. These paralyses are found to be associated with the destruction of the same parts of the cerebrum as the areas upon stimulation of which movements are produced. The paralyses, it is important to note, are inabilities to make certain definite types of combined movements, and not inabilities to move individual muscles. Thus there may be paralyses for extension and not for flexion. These defect phenomena vary with the part of the brain affected, those due to the internal capsule, and to the pyramidal tract below the latter being more diffuse.

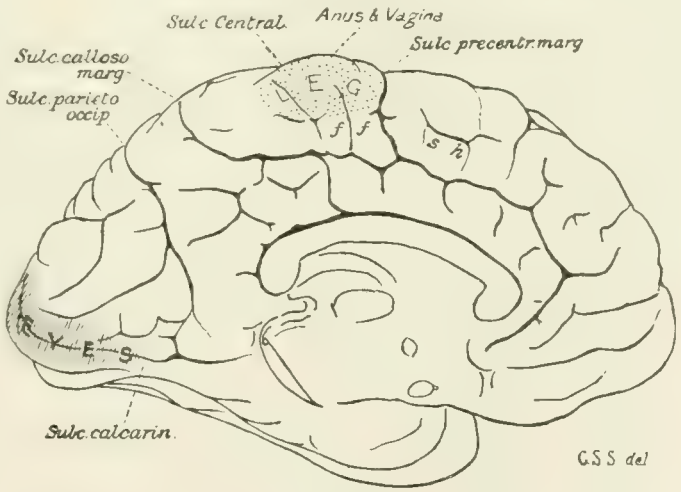
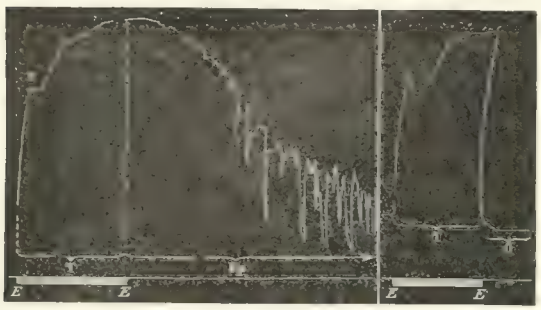


Fig. 1039.—Cortical Motor Areas on Mesial Aspect of Brain of Chimpanzee. (Grünbaum and Sherrington.) The calcarine area, marked with vertical lines and designated EYES, gave complex associated movements of these parts. The small letters indicate occasional and irregular movements of foot and leg, *ff;* of shoulder and chest, *s;* of thumb and fingers, *h*.

In only man and the higher apes are the paralyses entirely permanent, the effects being less and less marked as we go downward in the biological scale.

Associated with the loss of the ability to make

certain movements after destructions of parts of the brain, other secondary effects of these lesions are to be noted. At first the paralyzed part can be moved by external agents, but some time after the beginning of a paralysis the part which cannot be moved voluntarily becomes rigid and a contracture results. This contracture phenomenon is found only in man and the higher apes. A satisfactory explanation of the cause of the condition has not been advanced, and, in fact, there may be several factors operating in different individuals or in an individual at one time. Probably the most common factor is the loss of tone



A B

Fig. 1040.—The Production of Cortical Epilepsy. (From Schäfer.) Curves from a dog's muscle following strong stimulation of the cortex (*A*) and of the subjacent corona radiata (*B*). *E–E*, Periods of excitation; *T*, tonic contraction during period of stimulation; *Ep*, epileptiform contractions after the cessation of stimulation of cortex; *O*, absence of contraction after cessation of stimulation of corona radiata.

in the muscles affected and the overpowering effect of the antagonists, for where the muscles are equally affected, as in lesions of the peripheral nerves, this condition is not found.

Movement and the Occipital Lobes.—Electrical stimulation of the occipital cortex results in movements of the eyeballs and of the intrinsic eye muscles. The eyeball movements are associated movements and of a more complex nature than similar ones following stimulation of the precentral areas. Different observers have located in this region special centers for a number of movements, and experiments have demonstrated a functional connection between this region and the precentral cortex. Schäfer who has investigated this matter with great thoroughness reports: "If the electrodes are applied directly to the upper surface of the occipital lobe, conjugate deviation to the opposite side with downward direction of the visual axes is extremely well marked, and it is also produced by excitation of the mesial surface of that lobe, and of the quadrate lobule immediately in front of the internal parietooccipital fissure. If, on the other hand, the posterior extremity of the occipital lobe, its lower or tentorial surface, be stimulated, the lateral deviation is combined with an upward movement. In both cases the downward or upward movement may be almost uncomplicated by lateral deviation; this depends upon the position of the electrodes. On the other hand, there is an intermediate zone, narrow on the mesial surface of the lobe, and broader upon the outer or convex surface, excitation of which is productive of simple lateral deviation. All the effects are strongest upon the mesial surface, especially toward the anterior limit of the lobe; it is here that the local point for the movements is located." Von Bechterew, on the other hand, has been able to locate only three centers for movement of the extrinsic eye muscles and he has reported that eye movements may be obtained from the stimulation of the parietal lobe as well as from the stimulation of the occipital.

It has been found that eye movements may be produced by stimulation of the occipital lobe after the destruction of the precentral cortex, and by stimulation of the precentral cortex after the destruction of the occipital lobe. This has led some investigators to believe there are independent centers for the production of the eye movements, one in the occipital lobe, the other in the precentral cortex. This supposition is probably not correct, and the observations of Schäfer on this matter are of great interest and importance. He recorded the time of the latent periods of the eye movements following stimulations of the occipital and of the frontal lobes, and found that those produced by stimulation of the anterior part of the cerebrum were shorter than those produced by stimulation of the occipital cortex. That the lengthening of the time upon stimulating the occipital cortex is not due to the passage of the impulse from the occipital lobe, first to the frontal portion of the brain and thence to the muscles, is well shown by the fact that even after the extirpation of the motor area of the brain, the movements may be produced. That the impulses do not pass from the motor cortex to the occipital lobe and then on to the muscles is shown by the fact that they can be produced by stimulation of the cortex in the frontal region after the extirpation of the occipital cortex. On the other hand, from the results of the experiments on the latent periods of these movements, it is certain that there are more intercalated cells between the occipital cortex and the eye muscles than there are between the motor cortex and the same muscles.

Fig. 1041.—Curves Showing the Variations in the Latent Periods of Ocular Movements Following Stimulation of the Motor (Precentral) and Occipital Cortical Areas. (From Schäfer.) *Fr*, Frontal; *Occ*, occipital. Each dot indicates 0.004 second. Each latent period is the time represented by the horizontal marks.

Movement and the Temporal Lobes.—It has also been found that movements of the ears and head of an associated nature accompany the stimulation of the temporal lobes. These movements like those accompanying the stimulation of the occipital lobes have a longer latent period than those following the stimulation of the precentral cortex, and they may be produced after the extirpation of the motor region. Like the associated movements of the eye accompanying occipital stimulation, these movements are to be interpreted as the result of the transfer of the impulses from the temporal lobes to centers other than those in the precentral area, and the lengthening of the latent period indicates that the number of cells between the muscles and the temporal cortex is greater than that between the same muscles and the motor cortex.

Nerve Anastomosis and Movement Control.—A matter of both theoretical and practical interest in regard to cerebral function is that of the motor control after the operation of nerve anastomosis. It has been found that when, because of section of a nerve, a part of the body becomes paralyzed, the paralysis may be overcome by joining the distal end of the degenerated nerve with the central end of another motor nerve. Thus, Cushing made possible the return of function in the facial muscles by the anastomosis of the central end of the accessory nerve with the peripheral end of the facial. After about 300 days there was a complete return of function so that the voluntary use of the facial muscles was possible, although there was not a return of the reflex emotional expression function. This return may be explained in several ways. It appears that it may be due to certain new connections which take place in the

brain or to the assumption by one cortical area of the functions normally associated with another. It has also been supposed that there is an association (physiological and anatomical) of the facial sensory centers with the shoulder (accessory) area and that there is an education to bring about this functional connection as the usual and normal one. On the other hand, Cushing leans to the view that the facial centers influence or act upon the cortical centers for the movements of the shoulder and head by connection tracts through or subadjacent to the cortex, and in this way the movements of the face are to be explained as the effect of the activity of the facial motor area, which transmits its impulses to the shoulder area, and that thence the motor impulses travel to the appropriate muscles. Were the latter view the correct one, we should expect the return of function of reflex emotional expression as well as that of voluntary movement.

Motor Functions of Cortical Cells.—Some pathologists believe that the Betz cells are those from which the impulses arise which produce voluntary movements. These cells are found degenerated in cases in which there has been long-standing paralysis or extirpation of a limb, and the facts do warrant the acceptance of the view that these cells are closely associated with the production of movements of a voluntary character. There is, however, one fact which prevents the acceptance of the view that these cells are necessary for the production of voluntary movements, namely, that these cells are not to be found in the brain of certain animals, like the rabbit. There can be no question that voluntary movements may be performed by these animals even though the Betz cells are not found. It is well known that these cells vary in size, and attempts have been made to correlate these findings with functional differences. In this connection two hypotheses may be mentioned: first, that the size of the cells is correlated with the quantity of movement, and second, that the size points to the length of nerve fiber connected with the cells. The attempts to differentiate functional correlates for particular anatomical elements in the cortex has not been successful in this case, nor in the case of the sensory areas.

Motor Cortex and Spinal Cord.—It has also been shown that not only are the areas anterior to the central fissure concerned in the production of voluntary movement, but that they also have other connections or physiological associations with the spinal cord. The influence of this frontal region of the brain upon the reflexes in animals has been the subject of several investigations, the results of which may be summarized as follows: When the motor, and especially the frontal, cortex is extirpated the latent periods of the spinal reflexes become shorter than under normal conditions, and their intensity is increased, while the reverse effects are found when this region is stimulated, the reflexes having a longer latent period and the amount of the movements being lessened. Only slight effects of this character were obtained from the stimulation of other cortical areas, and it may be concluded, therefore, that the cells in this region normally act upon the cells in the spinal cord with an inhibitory effect. When in man the motor cortex is degenerated or destroyed or its connection with the spinal cord cells is interrupted, similar changes in the character of the reflexes are to be observed.

Motor Cortex and the Cerebellum.—It is well known that the cerebral cortex in the precentral region is connected by efferent fibers with the cerebellum. Some of these fibers pass to the contralateral and some to the homolateral parts of the latter organ. The pathway is from the cortex through the corona radiata and internal capsule to the crusta and the pontine nuclei, after which a division takes place, some passing directly to the cerebellum on the same side by way of the middle peduncle, while others cross to the contralateral side and also pass through the middle peduncle to the cerebellum. The motor cortex is also connected by means of some efferent fibers with the cerebellum by way of the thalamus, thence to the red nucleus and onward to the cerebellum through the superior peduncle, while others pass directly from the thalamus to the cerebellum through the superior peduncle. It should be noted, however, that some authorities dispute the passage of efferent cerebrocerebellar impulses by way of the superior peduncle, and affirm that the superior peduncle contains only cerebellifugal fibers. There appears, however, to be unanimity of opinion that the motor cortex is connected with both the homolateral and the contralateral sides of the cerebellum, and although there is some dispute regarding the paths, and although the exact functional nature of these connections is not well understood, it is apparent that in general the function is one concerned with the control of the automatic movements, *e.g.* walking, standing, etc., and perhaps also with general coordination.

Sensation.—Under the term sensation there are commonly grouped certain mental states which psychologically considered are more accurately known as perceptions. Thus, when we look at a table our sensations are those of light and shade of greater or lesser extent and of color, but our perceptions are of things, as a table, with papers, bottles of ink, pens, etc. Since in clinical and physiological work the distinction between sensations and perceptions is not usually made it is impossible to determine what defects have been found associated with cerebral lesions, but it may be added that histologists have freely used the terms sensory and perceptual to indicate supposed functions of certain areas.

The analysis of these states has shown that there are twelve or more different kinds of sensation. The older five-fold division into vision, hearing, taste, smell, and common or organic sensation is no longer held, for common sensation is now known to be a complex of different sensations. Among the best known of these are touch, pressure, pain, temperature, and sensations of movement. The relation of cerebral areas to all these forms of sensation has not been established. The general localization of the visual, auditory, gustatory, and olfactory sensations are known, but the localization of the different forms of common sensations is uncertain. This is the more remarkable since the spinal tracts for many of the latter have been established.

Vision.—Extirpations of certain cortical areas in the dog's brain which were accompanied by evidences of defective or lost vision, led Munk to the conclusion that in these animals there is a center for vision and that surrounding it there is another subsidiary visual center which can be used when the primary center is injured or destroyed. Goltz was unable to confirm these results, and although at first he denied that any localization was possible, later he was forced to admit a certain amount of localization was indicated by the results of the experimental investigations. The results following the extirpation of one occipital lobe have been variously reported and have consequently led to different interpretations of the connections of these cortical areas with the halves of the retinæ. Hitzig, for example, asserted that in the dog a lesion of the occipital lobe produced a crossed amblyopia, but this has been disproven, and to account for Hitzig's mistake it has been pointed out that the amount of the crossing of the fibers at the chiasm is greater in the dog than in the monkey and in man, two-thirds to three-quarters of one retina being connected with the opposite occipital lobe. Using monkeys as subjects, Ferrier located the visual area at first in the angular gyrus, but later, because of added results and criticisms of others, concluded that the occipital lobe was also used for visual sensations. In fact it was found by Schäfer that the angular gyrus may be

completely cut away without disturbing to the slightest degree the monkey's ability to see. It has also been well shown by Schäfer that when the lesions are limited to the occipital lobes, permanent visual defects occur. The condition found by Schäfer was that of hemiopia, not a contralateral amblyopia.

Chief among the results that have been reported on man are those of Henschen, who collated the literature on cortical blindness and reported personal cases. From the consideration of the clinical accounts and of the pathological and anatomical examinations, he concluded that the visual center in man is limited to the

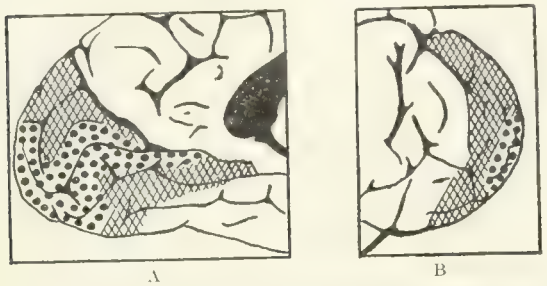


FIG. 1042.—The Occipital Pole of the Human Cerebrum, with the Areal Distribution of the so-called Visuosensory and Visuopsychic Regions. The dotted portions are the parts having the calcarine type of cortex, and the crossed hatched portions are the related parts of "visuopsychic" type. (Adapted from Campbell.) *A*, the mesial aspect, the dotted portion surrounding the calcarine fissure; *B*, the lateral aspect.

cortex surrounding and including the calcarine fissure, and that the centers for light and color coincide. He furthermore defined an area in the anterior part of the calcarine fissure which he assigned to the macula lutea, and disputed the conclusions of others who located the macular center in the cuneus. Henschen failed to find evidence in the clinical observations to prove a connection between the angular gyrus and the eye, although he believes that this area is concerned with visual processes, but of an undefined character, perhaps like that of perception.

There are many clinically reported cases which indicate that the localization of the visual area is not as limited as Henschen believes, and that the area concerned in vision is more widespread. Von Monakow has examined cases of early blindness and has found a widespread cortical degeneration accompanying these conditions, including not only the calcarine area, but a large part of the cortex on the convexity of the brain. The views of von Monakow were supported by Wehrli, who concluded that the visual area is not to be limited to the cortex surrounding the calcarine fissure, and not even limited to the part of the cortex with the cell lamination known as the calcarine type.

Following experimental extirpation of parts of the occipital lobes, several observers have obtained negative results, and have not been able to confirm the results obtained by other investigators. Vitzou extirpated parts of the occipital lobes and found that although the animals lost their visual ability immediately after the operation, the blindness was not permanent, and within a few months the animals learned to recognize objects and persons by means of vision. Similar results have been obtained by Panici, and in recent work Franz has shown that the lateral parts of the occipital lobes, which have the calcarine type of cortex, may be extirpated without changing the visual endowment of the monkey, although the destruction of the calcarine area is accompanied by true visual disturbances. The last-named observer found that other defects accompanied the destruction of the lateral parts of the occipital lobes; these defects being mainly those of a lack of coordination between the visual and motor processes; and he believes that the disturbance was due to a loss of certain sensations from the eye muscles rather than the visual sensations themselves.

Each occipital lobe is connected with the other by means of association fibers which pass through the posterior portion of the corpus callosum. When this region is destroyed or the functional connection is broken in any manner there is produced a condition allied to that of aphasia, which is known as apraxia. Here there is an inability to perceive through the visual sensations the meaning or use of certain kinds of objects, although the individual may still retain the ability to pronounce the words and have no other aphasic disorder.

The visual disturbances which accompany lesions of parts of the brain other than the cortex differ for the different locations of lesions. It is well known that when the retina or the optic nerve is affected there is an amblyopia for that eye. A lesion in the optic tract on the same side produces a hemiopia for the opposite field of vision (the inability to see with the homolateral parts of the retinæ). A lesion in the superior corpus quadrigeminum is not disturbing to visual processes *per se*, but a lesion in this location produces an inability to move the eye upon stimulation. This ganglion is connected in an efferent manner with the nuclei of the third, fourth, and sixth cranial nerves, and when the impulses cannot pass there results a paralysis or a loss of the associated movements for this part of the field. Thus we find

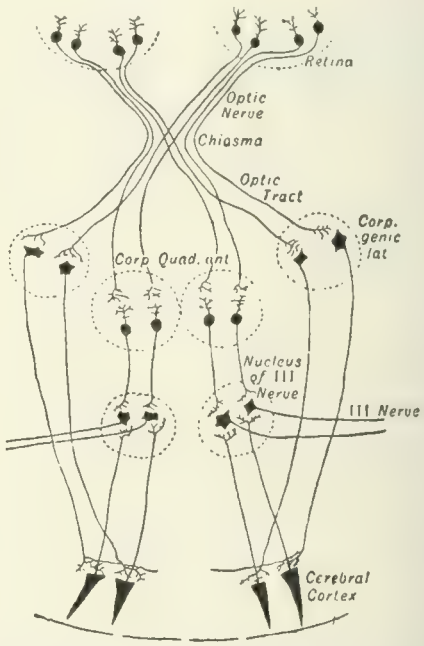


FIG. 1043.—Scheme of Impulses from Retinæ to Occipital Cortex and Nuclei of Cranial Nerves. (Halliburton, after Schäfer.) From each half of the retinæ two fibers are represented, one passing by way of the anterior quadrigeminal body, the other by way of the lateral geniculate body.

that the connection is made for both the intrinsic and extrinsic movements of the eye through the superior quadrigeminal body. Lesions in the geniculate body produce blindness very similar to those which are produced by destructions of the optic radiations or of the calcarine cortex.

The study of the degenerations has indicated that the connections of the eye with the remainder of the brain are (1) through the optic tract with the superior quadrigeminal body to the nuclei of the cranial nerves and (2) through the external geniculate body to the

cerebral cortex. Since the fibers from the nasal parts of the retinæ cross at the optic chiasm, we find on one side the geniculate body as a subsidiary station for corresponding parts of the retinæ.

It is found when the cortex is extirpated and the eye is stimulated by light, reflex movements are still possible, and since the impulses may pass to the quadrigeminal body and thence to the nuclei of the corresponding cranial nerves, these movements may resemble those which are found in normal animals. This is probably the condition that led some of the earlier investigators to doubt the cortical localization of vision in the occipital cortex.

Hearing.—The connections of the ear with the cerebrum are complex, many pathways being possible to the impulses which originate in the cochlea and travel to the cerebral cortex. It is likely that the impulses starting from one ear pass entirely to the opposite

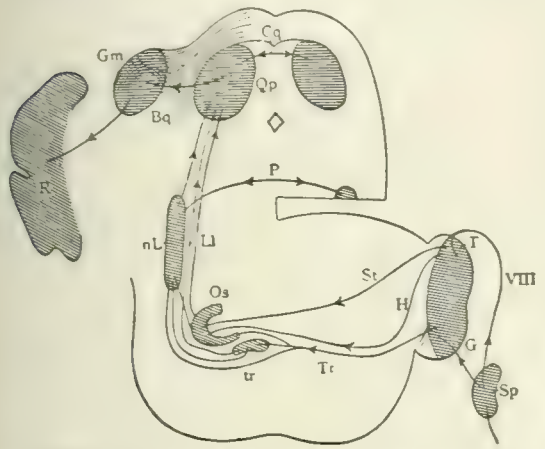


FIG. 1044.—Scheme of Impulses from Ear to Cerebral Cortex through Subsidiary Ganglia. (Stewart, after Lewandowsky.) *Bq*, Brachia of quadrigeminum; *Cq*, quadrigeminal commissure; *G*, accessory nucleus; *Gm*, corpus geniculatum medius; *H*, Held's fibers; *Ll*, lateral fillet; *nL*, nucleus of lateral fillet; *Os*, oliva superior; *P*, commissure of lateral fillet; *Qp*, corpus quadrigeminum posterior; *R*, cerebral cortex; *Sp*, ganglion spirale; *St*, striæ acusticæ; *T*, tuberculum acusticum; *Tr*, trapezium; *tr*, trapezoid nucleus.

hemisphere. The connections are made first through the accessory nucleus and the tuberculum acusticum, whence some fibers pass to the superior oliva on the opposite side, while others pass directly, and meet fibers from the superior oliva, into the lateral fillet. These fibers divide, some going to the inferior corpus quadrigeminum, others by the internal geniculate body whence fibers are sent through the internal capsule to the temporal regions of the cerebrum. Both cerebral hemispheres are mutually connected by means of association fibers which pass by way of the anterior commisure. Lesions in any part of the tract may produce disturbances of hearing, but there have not been collected sufficient data which warrant an accurate statement regarding differences in the auditory functions of parts subsidiary to the temporal cortex, viz., the tuberculum acusticum, the corpus quadrigeminum, and the internal geniculate body. On grounds of homology with the functions of vision we may expect that the internal geniculate body is concerned in the transmission to the cortex of the true auditory impulses, while the inferior corpus quadrigeminum may have a motor or efferent connection similar to that which exists for the superior corpus quadrigeminum.

It is known, however, that destruction of both temporal lobes in the brain of the monkey or of man produces complete deafness. Certain of the associated reflexes commonly found in connection with auditory stimulation may remain after such destruction. Animals which have been taught to react in special ways to particular sounds lose this ability after the destruction of parts of the temporal cortex and it may be concluded that this region has an auditory function, corresponding to the visual functions for the occipital lobe. Special differentiations of parts of this area have not been made, as has been done for the Rolandic and the occipital regions. Although some clinical observers have been inclined to believe that tones of different pitch were sensed through special parts, the facts are too meager to warrant acceptance.

Taste and Smell.—The difficulties in animal experimentation on these sensations are great, and there is little direct information regarding the cortical localization of these associated sensations. The connection of the end organs in the tongue with the cerebral cortex is doubtful, but that from the Schneiderian membrane is known. The impulses which arise in the olfactory cells pass through the olfactory nerve to the cells in the olfactory bulb, whence new impulses originate and pass mainly to the cerebral cortex in the hippocampal region on the same side, although some fibers go by way of the anterior commissure to the opposite corresponding cortex. The stimulation of the hippocampal cortex results in movements of the nostrils, mainly on the same side, and this fact has been interpreted as evidence of definite cortical representation of smell. Clinical facts regarding the localization of smell sensations are not numerous or important, the main one being that in certain cases of epilepsy with which are associated olfactory auræ lesions of the hippocampal region have been observed. It should be mentioned, however, that lesions in this region have been found in other epileptic cases which have not been accompanied by olfactory auræ.

Skin and Motor Sensations.—The relations of parts of the cerebral cortex to sensations which originate in the skin and underlying tissues are also not well understood. It is commonly believed that the postcentral and the intermediate postcentral cortex contains the cells concerned with these sensations, but differentiation of parts concerned with the individual sensations has not been made. Destruction of these areas in animals produces an ataxia which may, however, be caused by a loss of sensations very different from one another, but special experiments of a conclusive nature are lacking which will permit of the definite conclusion that this region is concerned with the sensations of movement or with those other numerous forms of sensations which are mediated largely through the end organs in the skin. That sensory losses accompany paralyses of cortical origin there can be no doubt, but in only a few cases have these been carefully investigated, and the dependence of particular forms of these sensations upon definite regions has not been established by the clinical findings. A few experiments on man have been performed at times when the skull was opened for surgical purposes, but the results are inconclusive. Thus in a conscious subject Cushing exposed the brain in this region and upon stimulation the subject reported sensations similar to those of a part of the body being moved. From this and other experiments it is apparent that there is a representation of some forms of sensation in this cortex, corresponding to that found in the pre-Rolandic region for movement. Clinical observations also indicate that this part of the cortex may be used for the skin sensations, for in cases of limited injury touch and pressure sensations have been found to be disturbed.

Brodmann, for histological reasons, divided this portion of the cortex into a number of quite separate areas, but in this was not supported by the observations of Campbell. Because of the histological discrepancies it is not possible to state the number of special types of areas, and we have no information regarding the probable connection of the various types

of sensations with this region, except in a very general way, as is indicated above. The close association of forms of hypoesthesia or anesthesia with paralyses indicates, however, that the sensations of touch, pressure, pain, temperature, and movement may have their representation in this postcentral area, but the facts are not sufficiently numerous and exact to warrant more than the general statement of this sensory control.

Association.—Although the loss of the ability to see or to hear is an intellectual defect, it has been usual to differentiate these elemental defects from the more complex ones of memories, etc. Although every cerebral process accompanied by a mental state is of an associational nature, the so-called higher mental processes are preeminently of this kind and the term association is physiologically used to describe those states which are believed to require the activity of more than one of the large cerebral areas.

The presence in man of general intellectual defects accompanying cerebral lesions and diseases, early led to the conclusion that the brain was the organ whose normal activity produced these mental processes. Later, clinicians attempted to correlate certain mental processes with special parts of the brain, and this led to what we now think an absurdity, the system of physiognomy of Gall and Spurzheim. That their hypotheses were disputed was partly due to the artificial character of their psychology and by this fact also may be explained why the views expressed by them did not receive due critical attention. On the other hand, because of religious and other preconceptions many disputed the dismemberment of the brain, and, like Flourens, contended that the brain was used as a whole in all mental operations, that no one part was used for any particular mental process, and that even though most of the brain were destroyed, the mental processes could be carried on very well with even a small part intact. The views of Gall, however, led to many observations and they were the means whereby other investigators were stimulated to observe and to contribute facts which have been found useful for the understanding of mental-cerebral relations.

Attention was early directed to the frontal lobes, since in man they are much larger, both absolutely and relatively, than corresponding regions in animals. Broca, Hitzig, and many others believed that the frontal lobes are concerned with the so-called higher mental processes, and much clinical evidence may be adduced to support this supposition. Collections of cases (by Welt, Phelps, and others) in which the frontal regions had been destroyed by accident or by growths have contributed to the belief in the supposition that the frontal lobes in man are the most important parts of the brain for the carrying on of intellectual operations. The mental changes accompanying frontal-lobe lesions have been variously described as: poor memory, loss of memory, inattention, mental slowing, mental deterioration, changes in character, incoherence, apathy, delusions, etc. Not all of these abnormal conditions have been found in each case, and many of the reported cases have included aphasic disturbances and delirious conditions which are known to accompany cerebral lesions very far from the frontal lobes and their value for an understanding of these regions is very doubtful. In fact, a careful examination of the symptoms in some of the cases cited in support of the view that the frontal lobes are intellectual centers shows that they have little or no value toward a settlement of the question, and, on the other hand, there are some cases of a negative character which have been used by the opponents of localization to show that large parts of the frontal lobes may be destroyed without a corresponding change in the mental capacity and general character of the individual. There are several well-reported cases which would lead to the conclusion that the frontal regions of the brain are no more important for the normal production of intellectual states than the posterior association areas.

On the histological side Campbell divides the frontal lobe into two portions, which he names respectively the frontal and prefrontal. The frontal area is highly developed in man both in the arrangement of cells and in the supply of fibers, and the prefrontal area is rather poorly developed both in fibers and in cells. Of the latter he says: "it can not share the functional importance of the better developed frontal cortex placed further back, and although it may have a future in front of it, at present its evolution both structurally and functionally is incomplete." In addition, Bolton, working with different material, largely pathological, pointed out that the anterior centers of association of Flechsig (the frontal lobes) are underdeveloped in all grades of primary mental deficiency and these parts also undergo atrophy in dementia. His conclusion is that this region is concerned with the highest coordinating and associating processes of mind.

The physiological evidences indicating particular functions for the frontal area are not numerous and are mostly inconclusive. Some investigators have used the term "idiotic" to describe the actions of animals when the frontal lobes have been removed, while others have said it is impossible to notice the slightest difference in their behavior and mental functions (Loeb). Experimental work by Franz on both cats and monkeys, by the method of training and determining the presence or absence of these acquired associations following the removal of parts of the brain, has given very definite information regarding the use of the frontal lobes. It was found that the removal of the frontal lobes produced a loss of habits in animals, and that such losses were not found when other parts of the brain were extirpated. Since these losses were not accompanied by sensory or motor defects the conclusion was drawn that these parts are normally used in the associational parts of such reactions.

Certain experimental results have been used to support the conclusion that the frontal region is not a center for intellectual operations in general, but for certain kinds of mental processes or states. Thus, because of the normal inhibitory effects of the frontal regions upon the reflexes, several observers have concluded that they are centers of inhibition, and in support of this hypothesis they cite the restlessness and unceasing activity of animals from which the frontal lobes have been excised. When we realize, however, that many animals become dull and somnolent after such an operation instead of being restless, from the standpoint of inhibition this should be considered evidence of an increased function. The evidence apparently counterbalances in this respect. Because of the associated eye and head movements found by a number of observers, and the respiratory and other rhythm changes described by Langelaan, the hypothesis has been advanced that the frontal lobes are concerned with the function of attention. It scarcely needs to be pointed out that Ferrier and others who uphold this view have confounded attention as a mental process with attentive movements. That the destruction of the frontal lobes does not produce a loss of the hypothetical faculty of attention is well shown by the results of the extirpation of these regions in animals and the animals' subsequent capability of reeducation (Franz). If these areas of the brain are concerned in attention, it should be expected that following their extirpation an animal could not attend to certain necessary external stimuli and that there would be no possibility of the acquirement of new habits or associations. The work of Franz shows, however, that this assumption is not true and that animals have the capability of acquiring habits after the removal of both frontal lobes.

As a general summing up it may be said that, balancing the evidence pro and con, both the clinical and the physiological facts point to a dependence of certain mental processes on the integrity of the frontal lobes, and that these parts are normally used in the production of associations, or in the act of learning. The evidence is inconclusive for the association of certain definite mental states with definite parts of the frontal lobes, and there is no physiological correlate known for the histological division of the larger area into frontal and prefrontal.

Of other mental processes which have been associated with other parts of the brain we have little information. The speech function is one kind of associational process which has received much attention, but this subject is at present in such condition that the information at hand cannot be used to support the definite localization of particular mental processes in particular areas. It appears probable, however, that there are areas lesions in which bring about incapabilities of association which are clinically grouped under the general term 'aphasia.' The recent work of Marie and his criticisms of the older aphasia doctrines make it appear probable that the first and second temporal convolutions and the supramarginal gyrus are areas normally concerned with the associations of speech. The consideration of this subject by von Monakow is most instructive since he groups the aphasias as distinct association disturbances and thereby indicates their general relation to cerebral functions. (See article on *Speech, Disorders of.*)

Other associational processes, as functions of other parts of the brain, which have not distinct motor or sensory functions, are not clear. Bianchi describes a parietal syndrome accompanying destruction of the areas behind the intermediate postcentral zone, but the only associational disturbances which he ascribes to lesions in these regions is that of astereognosis (*q.v.*).

From all the results which have been accumulated by clinicians and physiologists what is certain is that in the two large associational areas of Flechsig, the anterior and the posterior, (1) there are groups of cells which are chiefly concerned with the transmission of associated impulses from one part of the brain to another, and not with the immediate receiving of afferent impulses from the bodily periphery or with the originating of motor impulses, and (2) that whenever these areas are diseased or destroyed there results a more or less marked degree of disturbance of the association ability of the individual. That these phenomena may be interpreted in purely mental terms some clinicians and many physiologists doubt.

As a working hypothesis Franz has formulated the following scheme for the two large association areas: The frontal regions are known to be closely associated with the motor mechanisms in the cortex, and the posterior areas with the sensory elements. In each association of a type dealing with the so-called higher mental processes both of these areas are used, the posterior being the receptive area and the frontal the emissive area. The frontal area is connected with all parts of the motor zone and the two hemispheres are connected with each other through these areas so that the great number of adjustments required in civilization may be carried on by this connection. At the same time the posterior areas are the other connecting link between the hemispheres and they are also connected with all parts of the sensory areas, so that the impulses coming into one area from the periphery may have associations through it with all other areas and with the motor associating mechanism. This hypothesis helps toward an understanding of the apparently opposed clinical evidence in regard to the frontal lobe, and it also assists in the interpretation of certain phenomena which have been associated with lesions of areas close to the sensory cortical zones.

The Cerebellum.—In man the cerebellum is absolutely larger than, but proportionately not as great as, in many other animals. In man its mass is approximately one-tenth that of the brain, while in such animals as birds it attains a size as large as the cerebrum. In other animals it is almost rudimentary, *e.g.* in the frog. Little indication of the functions of this organ has been gathered from the study of its gross comparative anatomy, but the study of its connections with other parts of the nervous system has been of great value. For an understanding of its functions it is necessary to keep in mind some of the main facts regarding its anatomical connections. In general it is admitted that it receives afferent impulses from the periphery of the body and from the motor cortex of the cerebrum, and that it sends impulses to the cerebrum and the spinal cord.

The course of the impulses from the motor cerebral cortex to the cerebellum has already been described. Some cerebello-cerebral fibers pass to the contralateral red nucleus and thence by way of the thalamus to the cerebral motor cortex. Some fibers, apparently beginning in the nucleus fastigii pass to the homolateral corpora quadrigemina. Although no direct fibers pass from the cerebellum into the spinal cord, it is probable that there is an indirect connection by means of the red nucleus and the rubrospinal tract, and another similar connection by the passage of fibers to the opposite olivary nucleus, whence new fibers pass downward into that side of the spinal cord.

The afferent tracts to the cerebellum are better understood than the efferent. Some fibers which arise from the cells in the spinal ganglia pass partly into the posterior columns and through the gracilis and cuneate nuclei to the opposite side of the cerebellum. Other fibers coming from the spinal ganglia arborize around cells in Clark's column, whence new fibers pass by the direct cerebellar tract to the homolateral half of the cerebellum. Other fibers pass from the inferior oliva to the opposite cerebellar hemisphere, and fibers from the end organs in the semicircular canals pass to the pontine nuclei, and thence to the opposite side of the cerebellum. Several other tracts have been described, that for the superior quadrigeminal body being of greatest importance on account of its relation to equilibrium function.

From his observations Gall concluded that in the cerebellum was located the seat of the instinct of love and that the cerebellum was a center for the sexual organs and for the functions of propagation. This hypothesis has been almost forgotten, but its chief interest at the present time is that from the experiments of von Bechterew and his pupils the conclusion has been drawn that there is a rather close connection between the cerebellum and the functions of propagation and sexual activity.

The serious and systematical investigation of the functions of the cerebellum may be said to have begun by the experimental work of Rolando, which has already been described. The fact that the cerebellum could be stimulated electrically led Rolando to conclude that this organ is the source or the originator of the movements of all the voluntary muscles, but this view was not generally accepted. Flourens studied especially the effects of the destruction of the cerebellum as a whole and of its parts in birds, and because of his experiments concluded that the cerebellum is not a center for the production of voluntary movements, but that its chief function is in the control of those movements which are of a mixed voluntary and involuntary type, viz., those of an automatic nature such as standing, walking, flying, swimming, etc. Flourens found that in animals in which the cerebellum was destroyed "volition and sensation and perception persisted." The possibility of executing movements together also persisted, but coordination of movements was lost.

Luys directed attention to the fact that muscular

weakness is an immediate effect of the destruction of part or of the whole cerebellum, and the experimental work of Weir Mitchell led directly to the conclusion that in some manner the cerebellum was to be considered a source of energy for the motor centers in the spinal cord. Mitchell observed that the cerebellum could be irritated by chemical means and later

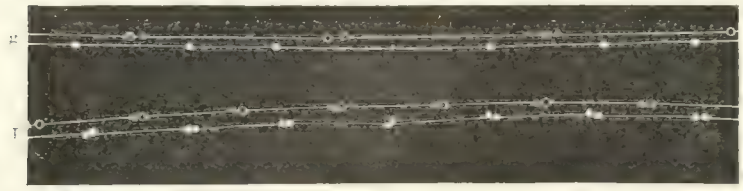


Fig. 1045.—Diagram of Footprints of Normal Dog: p, when walking g, when galloping. (From Luciani.)

Nothnagel found that the application of mechanical means to the cerebellum produces motor changes in the body. Mitchell also found that after the extirpation of the cerebellum there was a tendency to great bodily fatigue and in this observation we see the beginnings of our more recent views of cerebellar function.

From the observations on mammals, and from the results of Flourens' work on birds Ferrier concluded that the cerebellum is the center of equilibrium and of spatial orientation. It is both structurally and functionally closely connected with the semicircular canals, and the latter with the muscles may be considered the chief peripheral end organs which send impulses to the cerebellum. The hypothesis of Flourens, that the cerebellum is concerned with motor coordination, did not appear to Ferrier to meet all the facts and he denied that the cerebellum had a coordinating function in the sense that Flourens used the term. Certain facts gained from his own animal experiments and from clinical observation appeared to be against the view of a coordinating function of the cerebellum. The chief facts in this line are (1) that after the first few days following an operation coordination does take place, and the animal can coordinate its movements fairly well, or well enough for its ordinary needs, and (2) that in man there is associated with cerebellar lesions a loss of equilibrium, vertigo, and a lack of bodily orientation while coordinated movements can and do take place.

We are indebted to Luciani more than to any other for the careful analysis of the symptoms from cerebellar irritation and destruction. The facts that were found and utilized by Flourens and by Ferrier were known to Luciani and to these he added others that have been of assistance in bringing about a more careful analysis of the subsequently observed clinical cases. He noted, as had others, the decided motor derangement coincident with lesions of the cerebellum, but his investigations led him to a fuller analysis of this motor effect. He observed especially the failure in rhythm in voluntary movements and their lack of fusion. Many of the effects observed by him in animals, and those observed in man after cerebellar lesions, he showed could be accounted for when it is recognized that there is a decrease in motor power, and a lack of muscular tone. His explanation, therefore, of the motor disturbances is the one widely adopted at the present time, viz., that the disturbance is not a direct one, but dependent upon a lack of power or upon an asthenia. The asthenia is the cause of the astasia and of the cerebellar ataxia. The symptoms in cerebellar lesions are divided by Luciani into two classes, the results of different physiological conditions, on the one hand the defect phenomena and on the other hand the phenomena of compensation, *i.e.* the efforts at compensation for the defects. The asthenia, or muscular weakness, is the principal defect phenomenon and is the direct result of the loss of the impulses from the cerebellum. The attempts at compensation produce the main, and easily observed, motor deficiencies, viz., the isolation, the lack of rhythm and the incoordination of movements. In this attempted compensation the cerebrum plays the most important part.

The researches of von Bechterew and his pupils have given results similar in the main to those obtained by other investigators, but von Bechterew has made, by his use of all the available material, a careful analysis of the symptoms, more complete than that of Luciani because of the additional information he has had. He sums up the results of all the work in much the same manner as does Luciani, but in explanation of the phenomena returns to the earlier hypothesis of Magendie and of Ferrier. Von Bechterew gives three distinct symptoms due to cerebellar loss, these three according to him being the only phenomena due to the cerebellum directly. There are: (1) disturbance of harmony of the single movements in relation to the position of the body (astasia), (2) general muscular weakness (asthenia), and (3) a

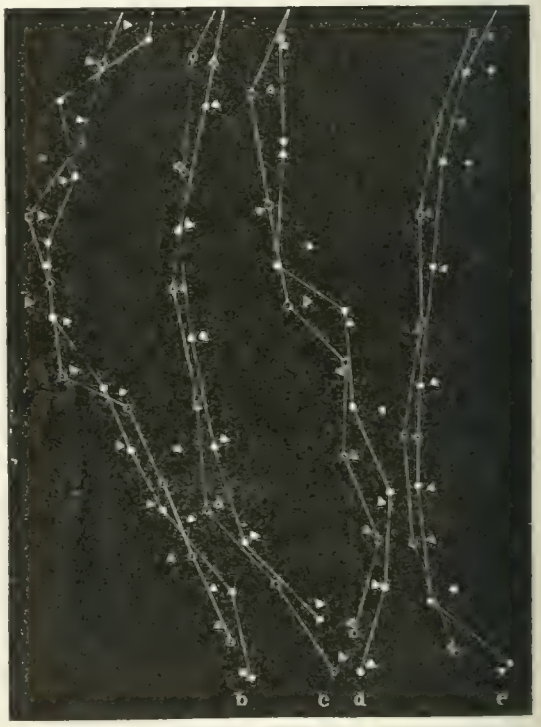


Fig. 1046.—Diagrams of Footprints of a Dog Ten Days after the Extirpation of the Middle Lobe of the Cerebrum. (From Luciani.) Compare with preceding figure, and note the marked degree of incoordination and the irregularity in length and direction of the movements.

decreased tension or atony of the muscular system. All these phenomena are believed to be of a reflector nature. They occur because of the loss of cerebellar function, or because of the abnormal stimulation of the organ, and they are increased by the impulses that arise from other parts of the nervous system, especially those from the cerebral cortex.

Only when there results the combination of the reflex activity with the impulses from the cerebrum do we observe the motor disturbances, once considered so characteristic of the cerebellum, viz., the rolling and turning movements, nystagmus, etc. The circus movements are, therefore, believed to be reflex; they are not due to motor impulses from the cerebellum or the cerebrum, but to impulses from other centers that are normally activated or reinforced or affected in other ways by impulses from the cerebellum. The reflexes arise from the association of afferent impulses from the labyrinth with motor impulses from centers situated in the region of the third ventricle, where are located the centers controlling static coordination. Von Bechterew lays considerable stress, both for the understanding of the physiology of the cerebellum and for the understanding of the clinical symptoms in man, upon the partial or almost complete recovery from the motor disturbances. With Thomas he believes that after the destruction of cerebellar substance the normal controlling action of the cerebellum is undertaken, as a sort of vicarious function, by the motor cortex of the cerebrum, although in certain cases in which the motor cortex is extirpated this function may be assumed by other lower motor centers. It appears, therefore, that not only are some of the marked symptoms of cerebellar disease caused by the activity of the cerebrum, but that at the same time the latter organ is able to compensate for or to replace to a certain extent the functions of the cerebellum.

Many recent investigations have tended to show functional connections of the cerebellum which earlier observations had not disclosed, and, in association with the more careful clinical studies, it has been shown that there is almost as much differentiation of the motor connections in the cerebellum as in the cerebrum, the lobulus simplex being associated with movements of the head, the crus primum lobuli ansiformis with the anterior extremity (steppage and movements of salute), the crus secundum lobuli ansiformis with the posterior extremity, and the lobulus paramedianus with the trunk movements (pleurothotonus, rolling movements, etc.).

Brief mention may be made of the similarity of symptoms from cerebellar and frontal lobe (cerebral) lesions. Unless the symptoms of static incoordination and of loss of equilibrium are marked, the motor phenomenon from lesions in both regions may appear alike. This similarity of symptoms may be understood when we consider that both these parts are concerned in the regulation, and not directly in the production, of activity.

The suggestion has been made that the stellate cells, the basket cells, and the granule cells have receptive and associative functions, and that the cells of Purkinje originate the coordinating impulses and those impulses which control the activity of the cerebral and spinal cord motor cells.

Although some have believed the cerebellum to be a center for mental processes, many who uphold a strict mental localization in the cerebral cortical areas have disputed this view, regardless of the similarity of the clinical syndromes from lesions of these organs. It is interesting to note that the hypothesis of subconscious mentality has been suggested, but the meaning of this term (subconscious) is very vague.

The Ganglionic Gray Matter.—On account of their location the experimental investigations of the basal ganglia are not very satisfactory, since the cortex either above or on one side must be extirpated before these regions can be reached, or electrodes for purposes of stimulation must be forced through the overlying tissues, thus bringing about a destruction of parts and possibly also a spreading of the stimuli. The extirpation of these regions is also difficult, and the results are not simple, since their extirpation involves other neighboring structures. The clinicopathological observations when these ganglia are affected, because of the anatomical relations of the parts, are not always simple, and it is only by elimination, combination, and variation methods that we are able to obtain any indication of the individual functions. The difficulties both on the side of experiment and on the side of the clinicopathological observations are very great, and definite statements cannot be expected regarding functions of these complex bodies. Some indication has been given of the anatomical connections of some of these nuclei with parts of the cortex, and it is known that the thalamus is in very close relation with the motor and sensory cortex surrounding the central fissure. On the other hand it is well known that the lenticular nucleus is closely associated with the motor cortex of the cerebrum, and this latter relation to such motor acts as phonation is described in the article on aphasia.

Caudate Nucleus.—The stimulation of either one of these nuclei produces violent movements on the opposite side of the body and the head. The movements are similar to those which are produced by the continued stimulation of the motor cortex, being epileptiform in character. When the motor cortex on one side has been extirpated for from two to four weeks, and the caudate nucleus on that side is stimulated, no reactions are obtained; if the stimulation is given to the other side movements result. It would thus appear that the motor functions of this nucleus are controlled by some action of the motor cerebral cortex, and that the nuclear cells do not act independently. It has also been found that stimulation of parts of this nucleus produces changes in the respiratory movements, but these may be only concomitants of the general motor effect, and not individual movements controlled by special connections of cells. Changes in the blood supply and in heart action have also been observed upon stimulation of this organ, and mechanical stimulation has been observed to be accompanied by an increase in the temperature of the body. In clinicopathological conditions abnormalities of movement have been observed, but the phenomena associated with these results were varied; sometimes vasomotor changes were found alone or with the motor, and sometimes only motor. Kirchhoff concluded from the examination of a case in which this region was destroyed that in it was located the center controlling the trophic conditions of the muscles.

Lenticular Nucleus.—The extirpation of the lenticular nucleus in animals has been found to be accompanied by a complete paralysis for voluntary movements (Nothnagel). Upon stimulation of the nucleus in many cases there have been found tonic convulsive movements in the contralateral extremities and the head, which makes it evident that this nucleus like the caudate nucleus, is associated with the production of movement.

Destructions or disturbances of this region in man result in aphasic or anarthric conditions, according to Marie, and lesions or irritative conditions of this part have also been found to be associated with states of abnormal motility, sometimes choreiform or athetoid. All of our knowledge indicates that this region is concerned with movement. Its definite relation to the motor cerebral cortex is not understood; it is not certain that movements are initiated by the lenticular cells, but it is probable that, like the caudate and cerebellar cells, the motor function is subsidiary to that of the cells in the precentral cerebral cortex. Recent work by Wilson indicates that its probable motor function is one of "steadying effect on the action of the corticospinal system."

Thalamus.—That the sensory impulses which pass upward from the cord to the cerebrum pass to the thalamus first is now well accepted. The thalamus, therefore, must be considered to be a sensory center,

and, as such, is probably subsidiary to the sensory cerebral cortex.

When the thalamus is destroyed there results a complete contralateral hemianesthesia. In pathological conditions associated with the destruction of this nucleus, there are found a number of symptoms of varied character. A patient with a lesion in this region is emotionally unstable, or, to put the matter in objective terms, such a patient expresses emotional states very easily. Continual spasmodic laughing or crying has been observed in patients with this part of the brain destroyed, and associated with these conditions we find fear.

Some cases have been observed in which disturbances of the thalamus have been associated with respiratory changes, and especially with the Cheyne-Stokes phenomenon. Vasomotor disturbances have also been noted in the contralateral extremities, and sometimes associated with these are edema and an increased temperature.

Von Bechterew has found that the stimulation of the thalamus in dogs produced changes in the sexual organs, such as contractions of the uterus and increased blood supply and secretions in these organs. The stimulation of the thalamus also produces a contraction of the pancreas and of the urinary bladder. Other experimental results have shown that the respiratory rhythm is changed and this finding is in harmony with the clinical observations. These results indicate some connection between the thalamus and motility, which is also indicated on anatomical grounds by the presence of the cerebrothalamic-cerebellar paths.

Lesions of the pulvinar give rise to visual disturbances on account of the interruption of the optic fibers, about one-fifth of which pass through this region.

The Geniculate and Quadrigeminal Bodies.—About eighty per cent. of the optic fibers pass by way of the lateral geniculate body, and this ganglionic mass is visual in function (see section on Visual Functions of the Cerebrum.) The medial geniculate body is part of the auditory path to the cerebral cortex (see section on the Auditory Functions of the Cerebrum). The superior quadrigeminal bodies are connected with the optic fibers on the one hand and with the nuclei of the III., IV., and VI. cranial nerves on the other, and are, therefore, reflex stations for the eye movements (see section on Visual Functions of the Cerebrum). The inferior quadrigeminal bodies are parts of the path of the auditory fibers, and they are parts of the auditory mechanism (see section on Auditory Functions of the Cerebrum).

Other Ganglionic Masses.—The functions of other groups of cells are to be determined only indirectly, by noting their degenerations following lesions of other parts. In this group we may mention the following: red nucleus, hypothalamus, substantia nigra. The functions of these parts are in doubt, but their anatomical connections give information of value in this regard (see article on Anatomy of the Brain). SHEPHERD IVORY FRANZ.

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Brain, Softening of.—See *Brain, Circulatory Disturbances of.*

Brain, Surgery of the.—Opening the skull by rude means seems to have been a prehistoric practice in many parts of the world. In the earliest days it may occasionally have been performed for consequence of injury or suspected disease, but is more likely to have been a rite practised in accordance with superstitions, or beliefs concerning the liberation of evil spirits, or for some other motive for whose hidden cause we have not here to seek. In ancient India, in Algeria, in Serbia, and in various other portions of the eastern hemisphere, as well as among the predecessors of the North American Indians, among the Peruvians, and many of the South Sea Island natives or colonies, museum specimens prove the more or less frequent observance of the ceremony or rite as it may have been (Figs. 1047 and 1048).

HISTORY.—In the history of medicine we need not for our present purpose go back before Hippocrates, who described the operation of trephining and who advised that one should not perforate quite down to the dura, but leave a thin layer of bone to the process of exfoliation, in order not to injure the membrane beneath. He, perhaps first, recommended, in order to prevent undue heating of the instrument by friction, to cool it with frequent applications of cold water; while others, later, recommended milk or oil of roses for the same purpose. Various forms of saws were in use from his day down to the present. Celsus recommended the cranial trepan (conical) which contained also the central pin. In his day it was customary to use a simple cranial or circular-saw trepan, and to

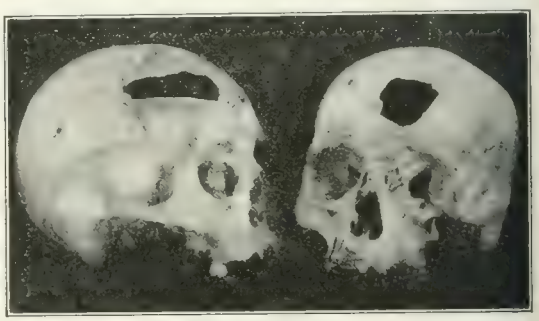

FIG. 1047.—Prehistoric Trephining; Skulls from Huarochiri. (Bureau of Ethnology.)

follow this with the pyramidal or conical instrument. Celsus also advised the practice of drilling a series of small openings around the margin of any piece of carious or dead bone which might require removal, and then to connect these openings with a chisel and hammer. He also introduced a sort of spatula or plate called the *meningophylax*, an instrument intended to depress the membranes in order to protect them. Various forms of chisel were in common use, as well as of forceps, for removal of portions of bone. All sharp bony projections were also removed. Celsus speaks particularly of prognosis, and of precautions to be taken in order to secure the most desirable cicatrices. Heliodorus recommended various positions of the head, usually with the patient sitting with his head between the knees of the operator. He advised that the ears be plugged with wool in order to lessen the sound of the instruments; also that a probe be used for investigation of conditions beneath the skull. He recommended dressings of charpie saturated with oil of roses. Galen recommended the use of the probe-pointed knife and of the *abaptiston* instead of the trephines then in use, this instrument being a trepan provided with a guard to

prevent too deep penetration. Paulus Aegineta practised the cross-shaped incision for exposure of the surfaces to be attacked, but advised delay of at least a day before actually attacking the bone, for which latter purpose he used mainly the hammer and chisel. Abulcasis employed the abaptiston, but bored numerous openings which he connected later either with the chisel or with a very stout knife which he seems to have devised for the purpose. Lanfranchi agreed with his Arabian predecessors, Haly Abbas, Avicenna, and Serapion, that it was unnecessary to follow up all fissures of the skull with the trepan, and that trepanation was practised unnecessarily frequently. Mondeville laid down twenty rules for use of the trepan, and advised that the dressings be saturated with warm wine, for which purpose he often used sponges. Guy de Chauliac used six different forms of instrument for perforating the skull. Vigo waited a day or two after opening the scalp, tamponing the wound before attacking the bony cranium. He insisted upon having his patients in a warm room. He noted the possible healings of fractures of the base, accompanied by bleeding from the nose and ears, without operative treatment. Cardano lamented the misuse, in his time, of the trepan, which he ascribed to the malicious avarice of the surgeon. Ryff seems to have gone back to prehistoric practices, *i.e.* to the time when the aborigines scraped through the skull with sharp shells or stone instruments, since he recommended perforating the bone with bone files, at least down to the internal table.

The great Paré treated fissures not so much with trepan as with the chisel or raspatorium, and usually waited two or three days before employing these. In his day, as before, all sorts of elevators with screw-shaped points, and, with tripods for their support, were in more or less general use, while cutting forceps were employed, as well as chisel and hammer, for removing points of bone. He described four indications for trepanation as well as six different points at which the instrument should not be used. Carcano Leone advised the use of cautery points for control of arterial bleeding. He was, perhaps, the first to suggest the use of pieces of bone for filling the defect, or the restitution of the bone already removed for the same purpose. He successfully opened the skull for intracranial hemorrhage, as well as for abscess. Glandorp quotes a case of Spighel's in which one patient was trephined seven times within a few days for consequences of injury, and yet recovered. He also quotes an instance of great protrusion of the dura which, when opened, gave exit to a large amount of pus. This patient also recovered.

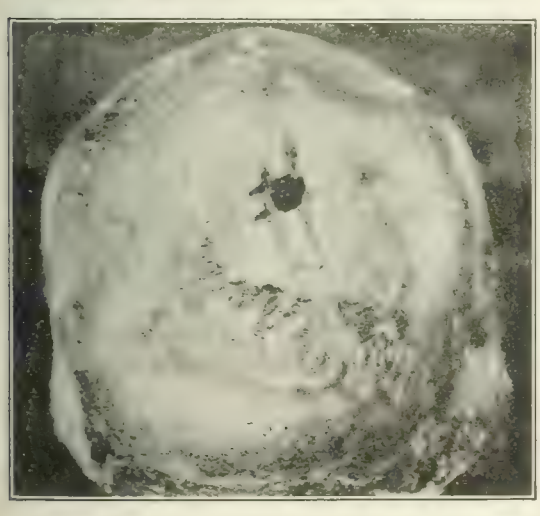

Fig. 1048.—Prehistoric Trephining; Ancient Peruvian Skull. (Bureau of Ethnology.)

Perhaps one of the earliest instances of opening the skull for posttraumatic melancholic insanity was that reported by Heinrich von Erfurt, of Cologne, during the thirteenth century. He operated with the patient in deep alcoholic narcosis, and described the opening as emitting a dense vapor (*grosser Dunst*).

Fig. 1049.—The Operation of Trepanning in the Early Part of the Eighteenth Century. (From Heister.)

Trephining.—*Preparation.*—Only a year or two ago the night before an operation was frequently quite as terrifying as the operation itself. With cathartics, frequent stools, and bowel washes, soap poultices, and irritating antiseptics, the hours were far from tranquil—and when with all this no breakfast was allowed, the patient usually went to the operation exhausted, both mentally and physically.

The night before an operation should be spent in sleep, and orders which necessitate waking a patient should be omitted. Personally we give our patients a light breakfast, usually a piece of toast with coffee, as without it some patients are very uncomfortable. An hour or two before going to the operating-room some drug should be given which will render the patient drowsy—or at least tranquilized—but in our opinion not sufficient to completely narcotize. Morphine is admirable, and whether it be combined with hyoscine or not is a matter of individual preference. Hyoscine in our hands has not been devoid of danger; while its action is beautiful when it works well, we regard it as a drug to be used very cautiously.

Chloretone, fifteen to twenty-five grains, given an hour previously, sometimes works effectively.

With a night spent in sleep, a light breakfast, and a mind relieved of concern, the patient is physically fit and mentally approaches the operation without fear.

We would not be understood as advising against preliminary eliminative measures—in fact quite the reverse—as we regard these of the greatest importance. Many patients come to the surgeon with dry skin, coated tongue, a frequent thready pulse, a loaded colon, with scanty high-colored urine. If there be time for such measures, certainly a week can very well be spent in thorough elimination. The night before

the operation is scarcely the time for them; but when time does permit, hot-air baths, bowel washes, and extra fluids are of great help. Except in cases of emergency, practically all our cases have a hot-air bed-bath the night before, as it not only causes liberal prespiration but causes the patient to drink copiously of water.

The local preparation here does not differ materially from the preparation of the skin in any other surgical operation. At the present time the tendency seems to be to return to the use of antiseptics in skin sterilization, iodine being the one in recent use. We cannot but feel that the preparation of the skin should include at least a cleansing bath, and, possibly, more extensive scrubbing. It scarcely seems justifiable to open the hairy scalp without at least getting rid of its ordinary accumulations. In operating on the head, whether this preparation be done before the anesthetic is started or not is of no material difference. Our preference would be for a close clipping of the hair the night before, followed by a thorough shampoo; the final preparation, after the anesthetic is started, to consist of a dry shave, followed by the application of iodine.

Preliminary administration of hexamethylenamine (urotropin) whose elimination by the kidney so alters it that the cerebrospinal fluid contains a very small amount of formaldehyde, is a precaution of very great value. When emergency precludes its use previous to operation it may be given immediately after it, even per rectum if necessary. For this means, doses of twenty grains (1.3 gram) in water are given at say four hour intervals during the 24 to 48 hours prior to deliberate operations; or in much larger doses if given by the rectum after its performance. It may also be introduced by spinal puncture.

In emergency cases dry iodine preparation is undoubtedly the method of choice, as time does not permit the usual scrubbing. If this be done it probably interferes with efficient action of the iodine. Where an open wound exists the simple application of iodine is preferable.

Shaving, ordinarily, is not very well done in a hospital, and with the implements at hand is usually a painful operation, and this is the chief reason for delaying it until after the anesthetic has been started.

Topography.—Every article on this subject seems to take up a detailed discussion of surface markings of the skull. What would we think if every article on abdominal surgery should include the topography of the abdomen? Dr. Cushing expresses it correctly when he states "that all neurological surgeons should know the brain as the abdominal surgeon knows the belly." When this is true it will scarcely be necessary for the surgeon to map out beforehand Reed's base line, the fissure of Rolando, and the fissure of Sylvius, as he will know where to make his incision with as much certainty as the abdominal surgeon knows where to make the incision for gallstones. For instance. he should know accurately the circulation of the brain, both that of the blood and of the spinal fluid, in order that he may more accurately appreciate their effect in producing compression, as also the surface markings of all the sinuses, with an accurate knowledge of the location of not only the centers of the motor area, but also those in other parts of the brain, the motor and sensory tracts, and the cranial nerves.

In the days when only a small circular opening was made in the skull, it was necessary to be exact in localizing exactly the motor area. Now—when large flaps are made—it is not so essential. A line is drawn from the middle of the orbit to the external auditory meatus, and a perpendicular from this line through the auditory meatus passes over the upper part of the motor area. This makes an easy landmark by which the motor area can be mapped out at a glance, and is of considerable help. For the usual discussion on the surface markings of the skull, the reader is referred to the article on *Cranio-cerebral Topography.*

Anesthetic.—There are a few surgeons who feel that chloroform has a special field in surgery of the head, but the principle is the same in this as in any other surgical work. This is not the place to discuss the general question of anesthetics; but, in the main, we believe ether is the anesthetic of choice. Nitrous oxide with oxygen has its special advantages, no clinic being complete without it, but in no sense can it be considered an anesthetic to the exclusion of ether. Nitrous oxide as a preliminary to ether has much to commend it, as it quickly puts the patient to sleep and relieves him of the early distress from ether. In spite of the extraordinary claims of the nitrous oxide enthusiasts ether must be given the choice as the safest anesthetic.

The intratracheal insufflation method of Meltzer, as modified by Elsberg, has proven to be of great advantage in surgery of the head, neck, and thorax. There

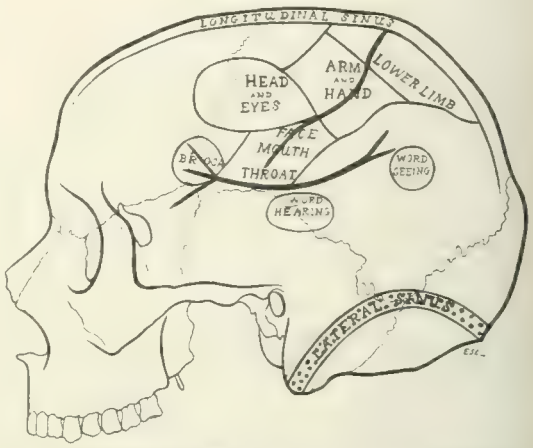

FIG. 1050.—Surface Markings on Skull, Showing Relations of Important Centers.

are several other modifications of this same principle, which doubtless are equally satisfactory. By this method of anesthesia the head of the patient can be entirely covered with towels and the anesthetist is out of the way of the operator. Furthermore, it has been demonstrated that this method supplies the patient with the oxygen necessary for life, whether he attempts to breathe or not; and this is of very great help in certain operations where it is difficult for the patient to breathe because of his position on the table. In operations on the base of the brain, performed through the nasal route, it is of the very greatest importance, because it prevents the blood from running down the trachea, it being blown upward by the escaping air.

Instruments.—The instruments used for opening the skull have been but poorly adapted for their purpose. The ordinary carpenter has tools in many respects better suited to his use than those employed by the surgeon in cranial work. The old circular trephine was most unsatisfactory. Many other instruments have been devised, but few are useful. Drills of all kinds are on the market, both with hand and electric power, but with most of them injury to the brain is not unlikely to occur. A few years ago Dr. Hudson, of Atlanta, introduced a hand drill which locked after passing through the bone, thus preventing injury to the dura. This has been exceedingly satisfactory in our hands, and has made the operation of trephining very much easier. He has also by his mechanical ingenuity produced cutting forceps which are far superior to any others we have used. These instru-

ments are almost a necessity for this work. (See Fig. 1051.)

Many of the electrically driven instruments are almost ideal in theory, but in practice inefficient. In the first place most of them are lacking in power; this, however, could easily be overcome. In the second place there is no adequate safeguard against injuring the dura, and this objection renders their use dangerous. The Gigli saw is used by some to connect the drill openings, but it so frequently breaks that it is of little benefit. Dural separators of various kinds are also on the market and are quite satisfactory. The hammer and chisel have been used a great deal in making osteoplastic flaps. From practical experience it would seem as though no harm followed or some special form which makes pressure on both sides of the skin over a larger area.

A device which has proved efficacious in controlling the oozing from the flap is to clamp the base with an ordinary intestinal clamp covered with rubber tubes. This effectually controls it without permanent injury to the circulation of the flap.

Technique.—A horseshoe-shaped incision is made over that part of the skull to be opened. The skin may be dissected back but is better left attached to the bone flap. It is desirable, however, that the periosteum be left attached to the bone unless the bone is to be permanently removed.

A small incision is made in the periosteum at each of the corners where the flap is made. An opening is

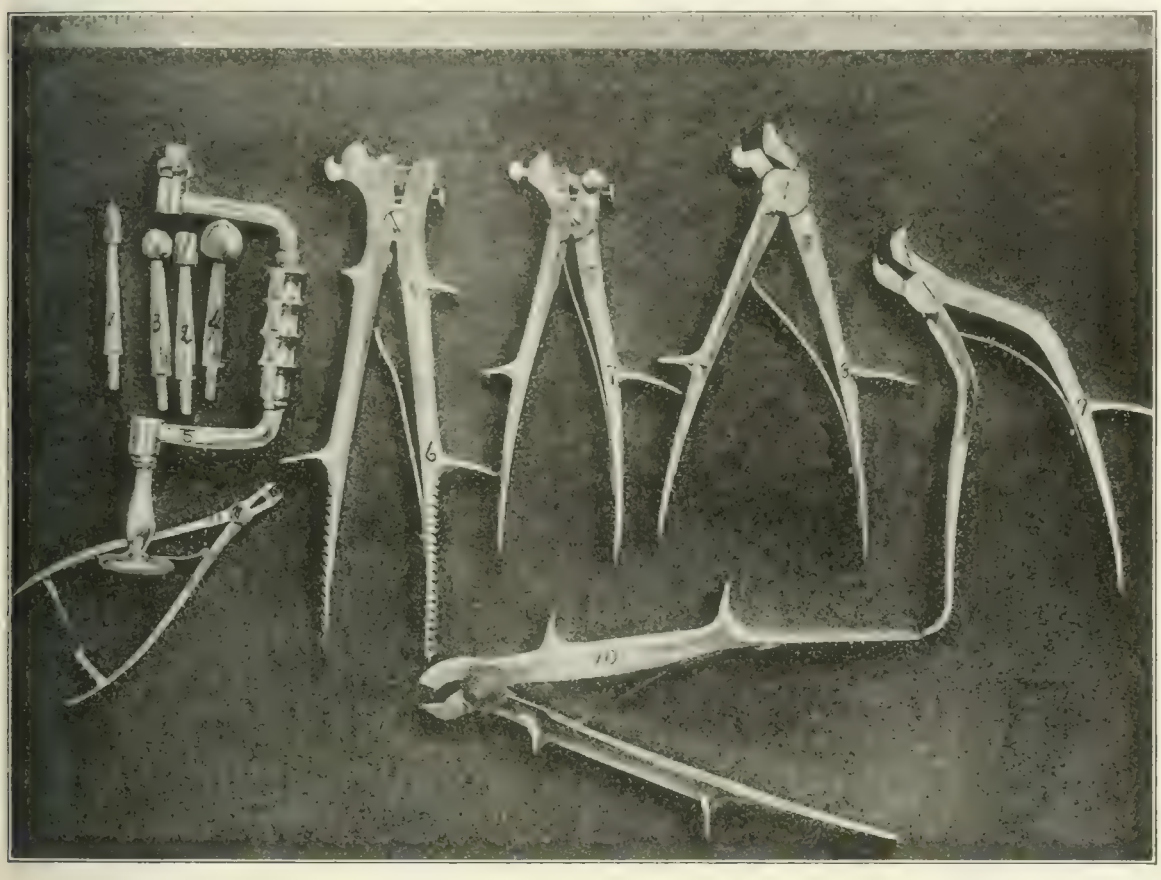

FIG. 1051.—Hudson's Instruments for Opening the Skull. 1–5, Trephine set; 1–4, burrs; 5, brace; 6, large two-handed cutting forceps; 7, same as 6, only one-handed; 8, large one-handed cutting forceps; 9, Hudson's most perfect cutting forceps; 10, large under-cutting forceps; 11, protector for drilling silver wire openings. (After Hudson; *Annals of Surgery*, April, 1913.)

their use, but in spite of this their employment ought to be extremely limited.

Hemostasis.—There have been many devices for the control of hemorrhage, but it is questionable whether any of them have proved of great value. That most commonly employed is the circular tourniquet, which can be used to shut off the blood supply of the scalp, but frequently when it is removed the oozing is quite troublesome, thus making its use of doubtful expediency.

Another method is to control the circulation by means of a circular suture surrounding the area to be operated. This, however, has the same disadvantage as the rubber tourniquet, in addition to the fact that it consumes more time in its application. We prefer to clamp the vessels, either by the ordinary hemostats

made with the smallest burr of the Hudson trephine. It is enlarged with the second one and made complete with the third and fourth. It is impossible to injure the dura with either of these as they automatically lock as they go through the bone.

The separator is now used to detach the dura from the bone, and the openings, save at the base of the flap, are connected, either by the Gigli saw or by the Hudson cutting forceps illustrated herewith. The DeVilbis cutting forceps was used a great deal for this purpose and in its improved shape is now an excellent instrument.

The base is now cut by chisel on each side so that, with a little force, a fracture occurs at this point. Ordinarily four openings are sufficient, but there is no objection to several more if thought best. Trouble-

some oozing from the bone can be controlled, either with gauze pressure, Horsley wax, or by forcing the edges of the bone together with pressure forceps, the latter being the much better method.

At this stage one should notice any peculiarity in the dura, either as to appearance, circulation, pulsation, or tension, as all of these may be factors in deciding whether or not it should be opened. If it is necessary to open the dura the incision should be fashioned like the letter W or M, especially where any great tension exists, as under these circumstances it is much more easily closed. (Hudson.) When tension is great we have used multiple small incisions rather than one large one, as it allows a stretching of the

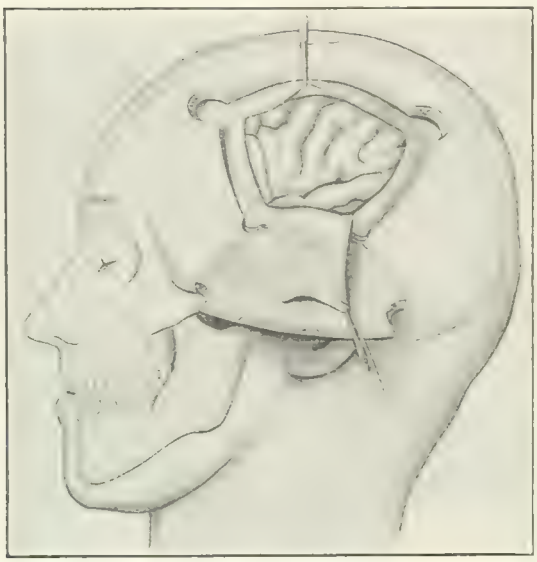

Fig. 1052.—Usual Cranial Exploration; Showing Osteoplastic Flap and Incised Dural Flap.

dura, thus relieving tension without necessitating closure. This is of especial advantage in cases for decompression, and will be spoken of under that head.

Gentleness in handling tissues must here be an inviolable rule. Centers when injured, even when partly excised, doubtless ultimately repair, but that is no reason for handling them roughly excepting under the greatest necessity. Even in needling the brain, to tap the ventricle or to explore for pus or other fluid, great care should be taken to avoid the centers, as irreparable harm may come from carelessness on the part of the operator.

Before closing the wound great pains should be taken to control all bleeding, as pressure may persist as the result of a retained clot. Furthermore, if there be any oozing which has not been controlled it necessitates drainage, and this is not desirable since it invites infection. In cases where there is no intracranial pressure the bone flap may be replaced without difficulty, requiring no sutures to hold it in place; but where intracranial pressure is marked, it may be necessary to fasten it in place by means of wire sutures. We prefer to close the skin with continuous sutures as this better controls oozing. In operations which are done in two stages, the flap is ordinarily closed loosely with either catgut or silk, in order that it may readily be reopened. The wound is dressed in the usual way, except that we envelope the head in a starched bandage, in order for a few days to limit its movements.

Decompression.—Much has been accomplished in brain surgery in the last twenty-five years, yet with few exceptions the end results have not been really satisfactory. For instance, in a recent review by Taylor, of Philadelphia, of 63 cases, there was a primary mortality of 30 per cent., the number including 14 complete removals, 9 partial, and 8 cysts. All of the patients were then dead save 5, and only two of these had reached the third year limit. This is a perfectly frank review and corresponds closely to the results of most operators in this work. To offset this there have been many other cases of very marked improvement, due solely to exploratory operations. Why this improvement took place is very difficult to understand, but it has occurred so often that it is now an established fact. Doubtless the reason in most instances is relief of pressure. In any event these operations have led to a more thorough understanding of the mechanism of compression and its relief through decompression. The operation of decompression is essentially an elaboration of the suggestion first made by Robert F. Weir, generally included under the term, "relief openings."

This has opened an exceedingly wide field; first, because most tumors cannot as yet be accurately localized; second, because even when accurate localization is possible removal is exceedingly hazardous; third, because in decompression we have a simple operation which is practically devoid of mortality, and at the same time quite effective in alleviating the most distressing symptoms of compression. In view of the fact that most compression symptoms can be relieved in this way, and of the discouraging outlook in cases of complete removal, it would seem that decompression should be the operation of choice in the great proportion of cases. In order successfully to decompress the brain we must appreciate the mechanism of compression, but unfortunately cerebral compression is not thoroughly understood. We can well understand how the usual causes, such as depressed bone, clot, tumors, etc., cause actual pressure on the brain, but these causes fail to explain many clinical manifestations of compression. For instance: following injury or operation, one occasionally sees a patient do well for a few hours, then slight twitching and jerking of an extremity occur, and later the patient grows so restless that it is almost impossible to keep him in bed. Finally stupor and death follow. This is a frequent picture of acute compression, for which there is as yet no satisfactory explanation.

The condition above portrayed is probably due to some interference with the circulation of the blood, causing edema. This may be due to obstruction of some of the larger veins, even to thrombosis of one of the large sinuses. The suddenness of the symptoms seems to point rather conclusively to an obstruction of the circulation rather than the mechanical pressure of bone or clot. One may be quite sure that in compression it is not so much the local condition as the damage done to the general cerebral circulation that produces the fatal outcome.

Again, one great trouble lies in the lack of elasticity of the skull. Were it not for the protection afforded by the hard bone we would be much better off with a covering which would change according to intracranial tension. Could we imagine a skull so formed that as intracranial tension increased the skull would literally expand, we would seldom see cerebral compression. The construction of the cerebrospinal canal does not permit of accommodation sufficient for such abnormal needs.

Granting these premises to be correct, the whole problem of decompression can be solved by an operation which permits the skull to increase in capacity in accord with increased intracranial tension. Viewed from this standpoint the usual operations are scarcely sufficient. At first the small circular opening was made; later a bone flap, and still later the subtemporal operation of Cushing. None of these gives greater skull content or capacity, but depends for its success

upon the development of a hernia. Furthermore, as the pressure becomes greater and the hernia increases in size, centers are compromised by the edges of the opening, paralysis supervenes, and the later condition of the patient is often worse than the first. If the dura be not opened there is little if any real relief from the removal of bone. Several times in cases of this kind, where the pressure was great, we have been mortified to see brain protrude so that it was impossible to replace it. Paralysis developed; with perhaps, later, infection and death. In the subtemporal operations these accidents are not so common, but in our experience, if the opening in the bone be small it fails in its purpose, while if sufficiently large, the fascia fails to hold the brain in place.

Krause, in his new work, speaks of raising an ordinary bone flap as the best way of relieving pressure. This can scarcely be correct, as in the presence of any great pressure one of two accidents will occur: First, the brain may protrude so that one cannot restore it inside the skull without amputation of the prolapsed mass; or, second, hernia may occur later, with paralysis, as the result of impingement against the edge of the bone.

The important principle in decompression should be, when displacement of the brain, due to release of pressure, occurs, that displacement shall take the direction where paralysis is most unlikely, and that direction we believe to be backward.

The usual decompression operation is that recommended by Cushing. His belief is that hernia of the brain is the logical way of relieving pressure, and the object ought to be to control this rather than combat it. Consequently he chooses the temporal area for such an operation; and utilizes the temporal fascia to control the hernia. A horseshoe incision is made over the temporal muscle, and the muscle fibers retracted. A circular opening is then made in the skull and enlarged beneath the muscle by suitable cutting forceps. The dura is then incised unless there is some special contraindication; then the retracted muscle is allowed to fall back in place and is sutured over the opening in the bone. This acts as a barrier to the hernia of brain which would otherwise occur, thus preventing the usual complication of paralysis from brain protrusion against bony margins.

The arguments advanced for this operation by that author are: (1) The frequency with which the lesion occurs in the middle fossa of the skull. (2) The fact that cerebral contusions are especially liable to involve the top of the temporosphenoidal lobe. (3) The exposure of the territory of the middle meningeal artery, and the ease of determining the presence of an extradural hemorrhage. (4) The possibility of draining through a split muscle rather than through the scalp. (5) The subsequent protection of the muscle against hernia. (6) The absence of deformity.

Unquestionably in decompression for fracture of the base, with slight pressure symptoms, this operation is almost ideal, for the reasons just given, but in decompression for tumor these conditions are different. Here it is simply a question of enlarging the cranial cavity in order to relieve compression, and in this instance we believe the operation of Hudson to be more rational; since the object to be obtained is to increase skull capacity, rather than produce a hernia. The opening ought to be made posteriorly in order to prevent paralysis. Dr. Hudson[1] advises that a large bone flap be made posteriorly, on each side, and that it then be held in place by wire sutures. These sutures are so lightly twisted that, as intracranial tension increases, the wire untwists, thus allowing the bony flap to yield, thereby increasing endocranial capacity.

The operation usually practised by us is based upon the same principles outlined by Dr. Hudson, but differing somewhat in detail. In view of the fact that so many tumors are inoperable, we believe decompression to be the operation of choice in the great majority of instances; especially so because of the difficulty of diagnosis between a cerebral and a cerebellar growth, or even between a left- or right-sided tumor. This decompression, to be ideal, should relieve pressure wherever it is manifest. A horseshoe incision is made posteriorly, from the mastoid to the top of the head, and down the other side, making the base of the flap just above the line of the transverse sinus. (Fig. 1053.) A bone flap of corresponding size is made, care being taken to avoid injury to the longitudinal sinus. There is no difficulty in raising this flap, if ordinary care is used in separating the sinus before breaking the bone. If a tumor be found above the tentorium, the dura is opened either by multiple incisions or by the M-shaped incision of Hudson[2] (Fig. 1054), and the bone flap is then replaced and held by wire sutures. In the event of pressure originating below the tentorium, the dura is separated, with care, below this point, precaution being taken not to injure the transverse sinus. With slight traction the cerebellum recedes so that the dura can be incised below the transverse sinus and over the cerebellum. If there be difficulty in this procedure the bone is further cut away without injury to the dura. Finally the bone flap is replaced in the same manner as above. The advantage claimed is the release of pressure obtained by thus enlarging the skull, instead of permitting hernia to occur. Furthermore, decompression is possible in both cerebral and cerebellar growths by aid of the same operation; and, lastly, parlaysis, that most unpleasant sequel of other methods, is here most unlikely.[3] (Fig. 1054.)

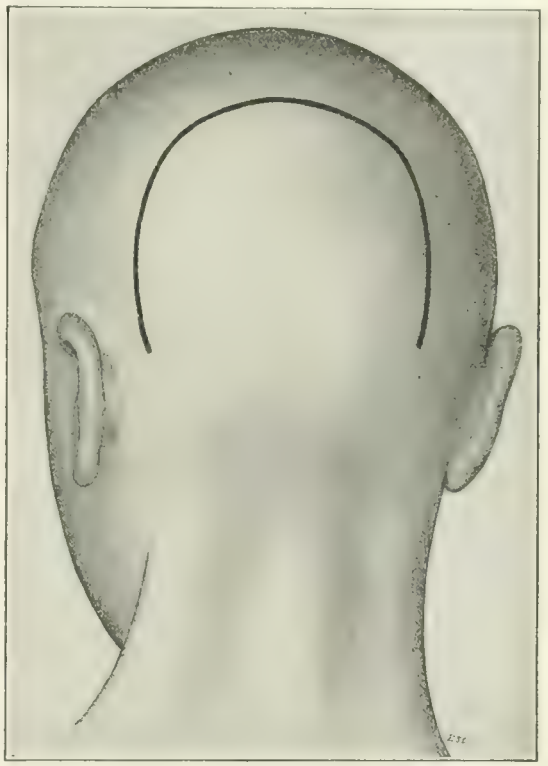

Fig. 1053.—Showing Skin Incision for McGuire's Decompression.

The usual decompression for cerebellar tumor has hitherto been that recommended by Cushing. The tissues posteriorly are retracted as in the subtemporal decompression, and the bone then opened. The opening is made larger by undercutting forceps; finally the tissues are accurately replaced to control hernia. This is usually accomplished by a T-shaped

incision, and the principle is exactly the same as in the subtemporal operation.

Abscess.—Infections of the brain may vary as do those of the peritoneum, from entirely walled-off collections of pus to a spreading infection of its membranes. The source of the trouble may be any pathway whereby infection can extend inside the cranium. Most frequently infections have their origin in

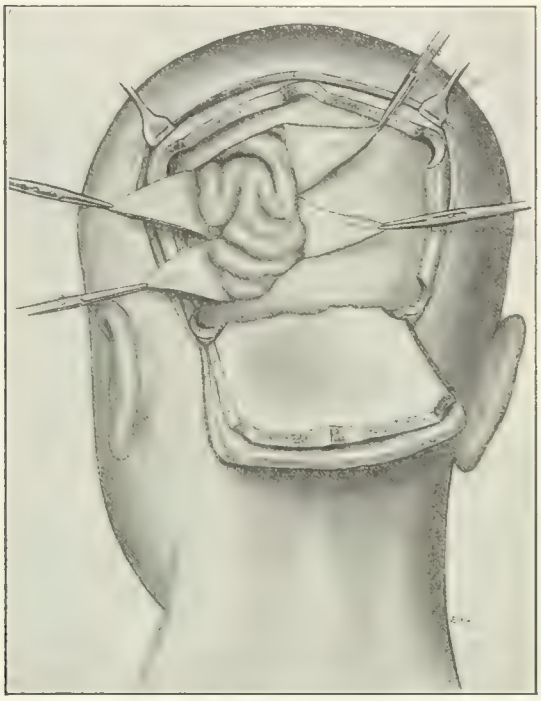

Fig. 1054.—McGuire Decompression. Large posterior flap. After separating dura below flap, cerebellum is retracted and dura incised below tentorium. M-shaped incision of Hudson in the dura.

middle-ear disease. Infections in the frontal area may occur from extension through the ethmoid and sphenoidal cells or the frontal sinus. A very frequent source of trouble, and one to be prevented if possible, lies in infection extending through recent fractures. It is not at all infrequent in such fractures, especially those of the base, to see patients do well for a few days—then infection is propagated through a fracture into the nasopharynx and death follows from meningitis.

In these cases prevention is almost the only successful measure. Where disease of the accessory sinuses is present it should be combated before infection of the brain can occur. While the use of urotropin is of questionable value in these cases, anything which offers any prospect of prevention should be used. All our cases of head injury are given this remedy in large doses, about 100 to 150 grains a day.

The operative procedure in abscess of the brain differs in no essential particular from that of trephining in general. It is usually wise to make a large bone flap over the suspected area; then, by a special needle, protected at the end to prevent injury to the brain, exploration is made in different directions. A special instrument of this kind has been devised by Murphy, so that by turning it slightly the point of the needle is opened, while by reversing the movement the opening is closed. Care should be taken here, as in the abdominal cavity, to prevent a spreading infection of the meninges.

In infected thrombosis of the sinuses the opening should be sufficiently large to permit one to clamp or tie the sinus on each side of the thrombus, before opening it. These cases are extremely serious and require radical work to be effective. In these infections urotropin has been highly recommended. It is usually given in large doses by mouth, but in

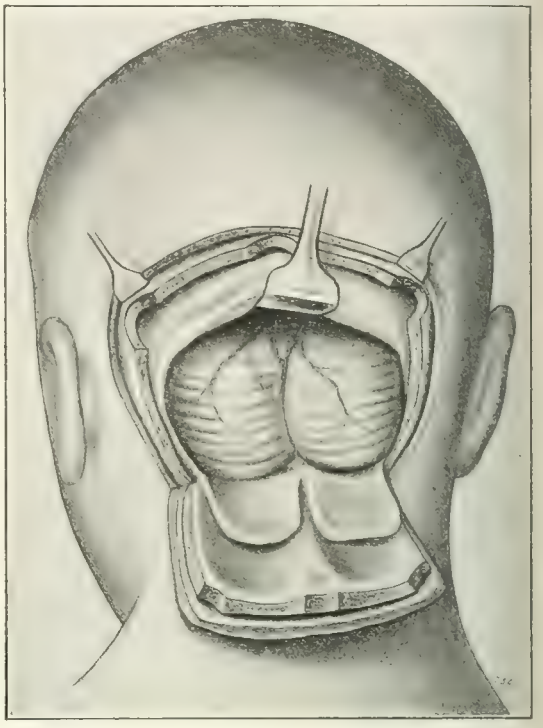

Fig. 1055.—Subtentorial Osteoplastic Flap Exposing the Cerebellum.

others it is injected into the spinal fluid through the ordinary spinal puncture. The latter procedure is well worthy of an extended trial, as anything which will prove effective in these cases will be a great boon, since they are nearly all fatal. There have been many suggestions whereby irrigation of the meninges may be attempted in these acute infections, but in our opinion none of them have met with any success. There can be no condition more serious or hopeless than an acute spreading infection of the membranes.

Tumors.—In view of the opinions expressed under decompression, we believe the operative work in this field should be largely limited to the operation of decompression. Radical extirpation may offer some hope, where accurate localization is possible, *e.g.* in cases of frontal tumors, those involving the motor area, the pontile angle, the cerebellum, and the pituitary. In *frontal tumors* and those involving the motor region a large bone flap is made over the suspected area; if the tumor is benign it may be possible to enucleate it without great danger to the brain. If it is malignant it will probably be inoperable, and it would be wiser to close the original opening and make a decompression operation posteriorly.

Pontile Angle and Cerebellar Tumors.—Here a large posterior bone flap is made over the cerebellum. If the tumor involve the cerebellum posteriorly there is no great difficulty in enucleation. If anteriorly, however, it is preferably reached by making a large bone flap exposing both sides, and by gentle pressure making a hernia of the other lobe, thereby

gaining more room. One will be astonished to see how much space can thus be made. This same procedure is of great advantage in pontile tumors as well. In any case great care must be taken to avoid making pressure on the medulla, as several deaths have occurred on the operating table from this cause. To avoid this, one needs plenty of assistance. (1) Intratracheal anesthesia is of great value. (2) An assistant should give constant attention to the blood pressure, and report its slightest change. (3) The pressure on the brain should be intermittent. If any disturbing factor present itself traction is immediately discontinued, thereby, relieving pressure upon the medulla. Most operators attempt the work through too small an opening, and are thus forced to use considerable pressure on the brain; this is a fatal mistake, and one should

Fig. 1056.—Cerebellar Exploration; Showing Cerebellum Retracted Exposing Tumor.

therefore err on the side of too large an opening rather than too much pressure. The pressure that can be made upon the brain will vary with the length of time and its extent. The time is placed anywhere between four and ten minutes, although this in some instances is too long. However, there is a degree of pressure on the brain beyond which recovery does not take place. In these operations, while no accident may occur on the table, patients may die later from no other apparent reason.

Gasserian Ganglion.—In operations for facial neuralgia, such good results follow the injection of alcohol that this ought to be tried in every case before exposing the patient to the risk of so serious an operation as the removal of the ganglion. There are two methods of approach that are in fairly general use; the temporal flap, elevating the brain from the side, and the large frontal flap, reaching the branches of the nerve from before backward. Usually this operation is regarded as one of the most difficult in surgery. The greatest cause of trouble is in trying to do the work through a small opening. A large opening renders the whole technique of the operation easy of performance, beside preventing the chief cause of death—namely pressure. A large bone flap is made over the temporal region, making its base on a level with the zygoma. The diameter of the flap in its largest dimension should not be less than three or four inches. With gloved finger covered with gauze, or a blunt forceps covered with cotton, the dura can be easily separated as far as the roughened part of the anterior fossa. It is usually safer at this point to separate the dura from before backward, as in the other direction injury to the middle meningeal, as it passes through the foramen spinosum, is quite likely. By very slow separation of the dura at the exit of the branches of the nerve it can, with some difficulty, be pushed backward, thus exposing the ganglion. Through the upper opening the first division must be separated from the fourth and sixth cranial nerves. The second division passes through the foramen rotundum alone, while through the lower one, the foramen ovale, passes the third division, it being only essential to divide the sensory branch. If the dura have been thoroughly separated the ganglion will be readily seen, and division posteriorly is possible. Otherwise the three branches are caught in a hemostat, and, by twisting, the ganglion is evulsed. The greatest difficulties will be, first, hemorrhage, and second, securing sufficient light so that the field can be easily seen. If the opening be large enough these difficulties are both obviated. No preliminary ligation of the carotid is necessary, as, if the middle meningeal is avoided, only venous oozing can occur. This can readily be controlled by packing against the hard skull. After division of the branches some foreign material is placed between the ends in order to prevent transmission of impulses later by union of the nerve; small pieces of oil silk, rubber tissue, wax, and paraffin have all been used for this purpose. If accurate division has been made and thorough removal of the ganglion accomplished, these will be unnecessary.

Regarding the arrangement for throwing light into the wound when necessary, a long curved glass rod with good illumination at its outer end, is admirable. A solid glass rod with its base against a small lamp can thus be made to throw a brilliant light into the field. It should be sufficiently curved so that it may hang over the edge of the wound without obstructing the view. The usual arrangement of head mirror and light is most cumbersome, and of far less value.

Apoplexy.—The operative treatment of intracranial hemorrhage in any form will vary largely with the type of bleeding. Hemorrhage may occur at any point, due to weakened vessels, and may be of any amount. The damage will vary according to these two conditions. For instance a small clot occurring at the internal capsule may produce more disturbance than a large one located in one of the silent areas of the brain. Hemorrhage may be extradural, subdural, or intracerebral. Of course it may occur anywhere inside the cranium, but this classification will ordinarily suffice.

The operative treatment will consist in raising a large bone flap, when, if the clot be *extradural*, it can be easily removed, especially if the opening has been made over the lesion. Even in certain cases where the hemorrhage has occurred at the base, there may have been sufficient separation of the dura upward to make it easily accessible from a temporal flap. If the hemorrhage be *subdural*, the treatment is more difficult because it is often diffuse, and more difficult of access. In those cases where it is impossible to locate accurately the source of bleeding, and where no local collection of blood exists, it would be better simply to make a decompression operation. *Intracerebral hemorrhage* may vary from a large hemorrhage occurring in a tumor to a very slight oozing at the internal capsule. If the bleeding be high, near the cortex, it can safely be evacuated. If bleeding occur in a tumor, decompression only should be done. In capsular hemorrhage, *i.e.* apoplexy, much depends upon the size of the clot. To quote from Cushing—by a proper

and guarded approach which avoids the insula and which is conducted directly through one of the convolutions, such a clot may be safely tapped, its cavity emptied, the immediate danger of compression may thus be warded off, while the removal of the clot will in all probability greatly lessen the paralysis.

Surgery of the Hypophysis.—The hypophysis which fifteen years ago was to the surgeons *terra incognita* is now frequently attacked, conditions justifying this consisting of tumors and symptom complexes indicating hyperpituitarism. Operative methods have been studied out on animals in which subtemporal methods have been employed, it being

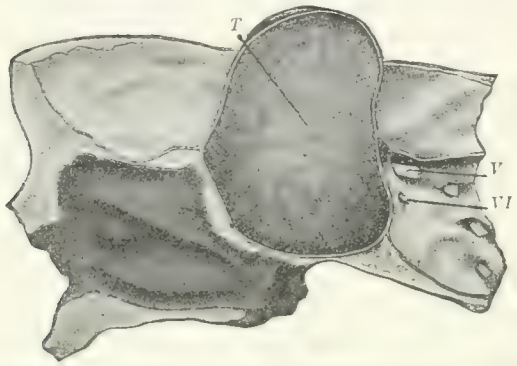

Fig. 1057.—Adenoma of the Hypophysis; Sagittal Median Section. Showing the projection of a pituitary tumor into the cranial cavity. *T*, tumor; *V, VI*, fifth and sixth cranial nerves. (After Schloffer, Beiträge zur klinischen Chirurgie, vol. I, 1906.)

more easily possible thus to guard them against infection. In human beings this is but one of the several possible methods of approach.

Before studying these it is wise to speak for a moment of the choice of anesthetic adapted in this particular class of case. By the rhinologists, who are accustomed to it, local anesthesia, usually with cocaine, has been employed even for the complete endonasal and transphenoidal operations, but these are, of necessity, slow and scarcely acceptable to the general surgeon; moreover they prolong the procedure and increase the difficulties encountered. A preliminary tracheotomy has been urged by some in order that the pharynx may be packed and hemorrhage better controlled; this also complicates any method employed, though it may be necessary with acromegalics with very large tongues. Now that the endotracheal method of Elsberg and others has proved itself so effective and so reliable it should certainly be the choice of those who are equipped with the apparatus, as, in fact, everyone should be who essays this operation. This will far exceed in usefulness the (tube) apparatus of Davis, etc.

Decompression is the primary object of every operation upon the pituitary, whether it be for tumor or symptoms of overactivity, because pressure symptoms compose a large proportion of the trouble to be relieved. When no other expedient seems practicable or preferable the ordinary subtemporal decompression, which may be made bilateral, may be employed. This may suffice, or may prove the imposed limit, or it may be a preliminary operation to be followed by more direct attack. Doubtless there are many cases which demand and will be benefited by both. Cushing favors the temporal method in certain cases, considering that after it there is a better chance for radiotherapy. Cranial decompression may, also, be demanded, and may suffice for relief of severe headaches and especially also after optic atrophy has already occurred and there is no choked disc to serve as a guide. Regarding many cases of overactivity, as due to the formation of what has been most properly considered a pituitary *struma*, we find the same justification for partial extirpation that we do in hyperthyroidism, as seen in exophthalmic goiter.

Decompression was first suggested by Schloffer, to check the progress of acromegaly, and has given excellent results, especially if followed by partial extirpation. But in the progressive cases rather than the stationary, and after involution has presumably taken place, and when neighborhood symptoms are increasing, any form of decompression alone may afford great relief. It is impracticable, usually impossible, to expose and completely remove an interpeduncular tumor, whether it be a pituitary struma, which has burst its confines, or an extra pituitary *anlage*. In these cases all that can be done will be to divide the capsule and remove a portion of the growth, as well as to remove the sellar floor, so that any further growth which may take place shall be encouraged in the downward direction and into the sphenoidal box.

Thus it will be seen that no one method is universally applicable and that each case must be studied and attacked upon its merits or demerits.

Routes of Access.—As stated above the method of choice in animals is the intracranial, not only because infection can be better prevented, but because here one deals with normal conditions and without increase of tension. Operations upon human beings

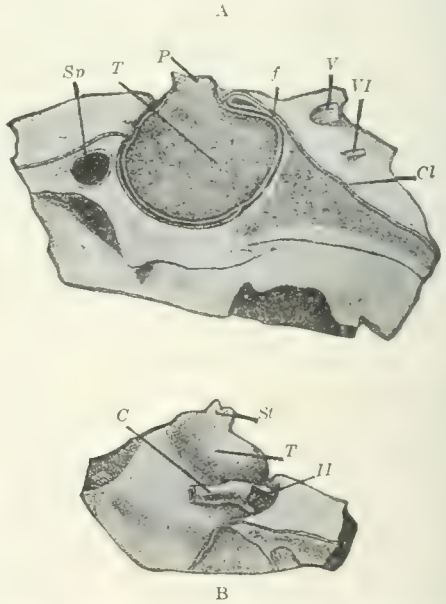

Fig. 1058.—Adenoma of the Hypophysis, Showing the Projection of the Tumor into the Cranial Cavity. A, median section; *T*, tumor with pedicle (*P*); *Sp*, sphenoidal sinus; *Cl*, clivus; at *f* is a fracture of the slope of the saddle reduced to the thinness of paper; *V VI*, fifth and sixth cranial nerves. B, the same seen from the cranial cavity; *C*, carotid; *II*, second cranial nerve.

are to be grouped under two general headings, namely, the intracranial, and the transphenoidal, though the two may be combined either in one or two stages. When the tumor is large enough apparently to prohibit sufficient and safe cerebral dislocation, with the requisite orientation and approach, then one may be compelled either to go through the sphenoidal body, or to combine both methods. Decision in this regard will be reached mainly by a study of a well-made skiagram and estimation, thereby, of the size of the sella turcica.

The intracranial method, though first suggested by Horsley, was first practised, in 1893, by Caton and

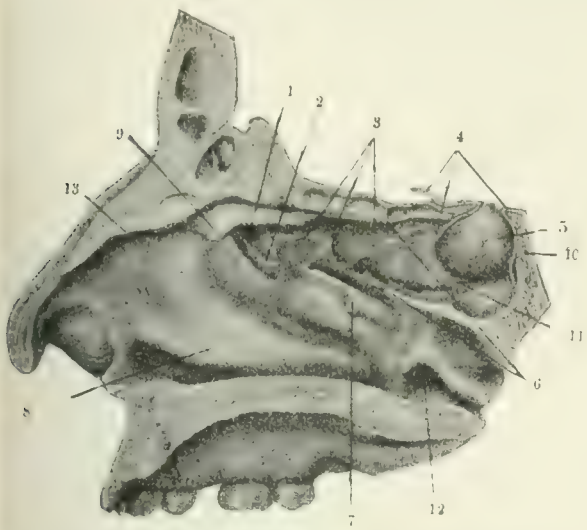

FIG 1059.—Endonasal Operation by Wide Opening of One Sphenoidal Cavity Only. Right half of the nose with the hypophysis tumor *in situ*. The bony shell of the tumor is removed, the dura split and turned aside. 1. Uncinate process. 2. Bulla ethmoidalis. 3. Remains of the ethmoid cells. 4. Dura. 5. Hypophysis tumor. 6. Margins of the widened sphenoidal cavity. 7. Posterior end of the middle turbinate. 8. Inferior turbinate. 9. Remains of the middle turbinate. 10. The back of the sella. 11. Sphenoidal sinus. 12. Opening of Eustachian tube. 13. Remains of the nasal septum. (After Hirsch; Voorhees, *Medical Record*, Aug. 17, 1912.)

Paul, although they added to the temporal operation an evisceration of the orbit. Anatomical abnormalities, such as an exceedingly overhanging brain, may make this the only feasible project. In 1905 Krause proposed a frontal approach, *i.e.* by large double or bilateral resection of the frontal bone, with ligation of the frontal sinus, and elevation of the frontal lobes. This has been done but a very few times, and requires very great dislocation of the forebrain. In numerous instances a lateral method of extirpation has been attempted and the complete operation abandoned for a decompression. This general method is more indicated in those cases which present marked neighborhood symptoms, and where the *x*-ray shows a fairly normal sella.

It must be remembered that the hypophysis is covered by neither arachnoid nor pia, but lies between two layers of dura. Therefore the subarachnoid space is not opened when these operations are properly performed.

Transphenoidal Route.—This also may be divided into the superior and inferior nasal methods; the former includes an osteoplastic resection of the anterior wall of the frontal sinus and the nose after the fashion first proposed by Giordano in 1897, improved nine years later by Schloffer, who also combined it, when necessary, with an extracranial or intracranial method. On the other hand the buccosphenoidal method, first proposed by Koenig, in 1900, namely, a separation of the superior maxillæ, and removal with chisel of the hard palate, has found more favor since Loewe, in 1905, proposed a separation of the maxillæ, but with much less displacement of the nose; but both of these have yielded to more recent and improved methods. Von Eiselsberg modified these methods with his so-called, tuning-fork incision, which is more nearly Y-shaped, on the forehead, with lateral wings carried along the nose, with resection of the frontal sinus and exenteration of the nasal cavity. Later he modified his first method by limiting it to incision on one side of the nose. All of these methods either opened up or sacrificed the ethmoidal cells, exposing, thereby, to greater danger of infection and meningitis; moreover they sadly mutilated the face, and interfered with, or destroyed, the sense of smell. Kanavel, therefore, suggested to turn up the nose, and expose the sphenoidal body by removal of the turbinates and part of the septum. In 1910, Hirsch proposed a simpler endonasal, transphenoidal route, doing the operation in two, or even three stages, beginning with primary resection of the septum and subsequent sphenoidal exposure through one nostril (Hajek); this gives fair access to the sellar base, and has been done even under local anesthesia. To A. E. Halstead, in 1910, we owe the suggestion to adopt a sublabial and infranasal incision, and this is the one now quite generally employed.

Before describing at least some of these operations more minutely, let it be emphasized that the preliminary administration of a number of doses of urotropin will materially reduce danger from septic meningitis, since it is known to be excreted by the membranes and thus to medicate, as it were, the cerebrospinal fluid with a reasonably active antiseptic.

Cushing's Combined Sublabial Transphenoidal Operation.—Inasmuch as the following method described by Cushing would seem to meet the indication in the majority of cases, and to combine both the simplest and most effective procedures, it will be described in some detail, with such brief allusion to other methods as may be called for, in order to meet departures from average cases.

When there is evidence of great intracranial pressure, and this can be ascribed to cerebrospinal fluid in excess, it can, if desired, be relieved temporarily by lumbar puncture previous to the major operation.

In practically all operations upon the hypophysis the head is placed in the somewhat modified Rose's position, being elevated and at the same time tipped backward. The posterior nares are plugged by sea-sponge, and then with pledgets of cotton wet with

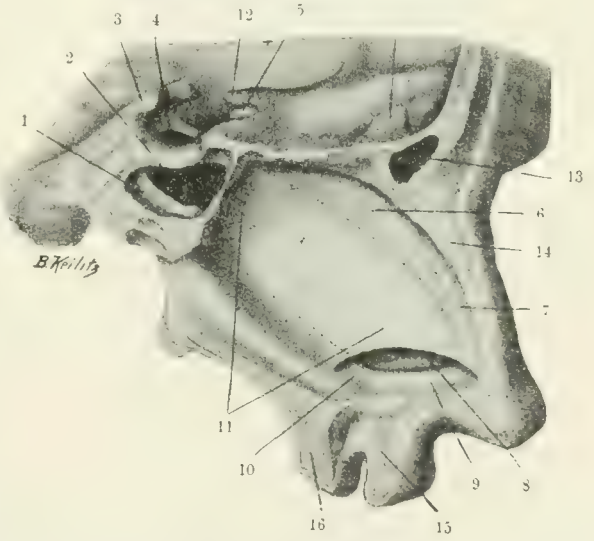

FIG. 1060.—Endonasal Operation by Submucous Resection of the Septum. (The skull was sawed through to the right of the middle line so that the entire left sphenoidal cavity is seen and a part of the right.) The septum between the two cavities has been removed in great part. In the floor of the sella (normal) an opening has been made. 1. Remains of the sphenoidal septum. 2. Left sphenoidal cavity. 3. Proc. clinoidei post. 4. Opening in the floor of the sella. 5. Optic nerve. 6. Lamina perpendicularis of the ethmoid. 7. Septal cartilage (upper margin). 8. Septal mucous membrane of the left side. 9. Septal cartilage (anterior margin). 10. Anterior end of vomer. 11. Septal mucous membrane of the right side. 12. Proc. clin. anter. 13. Frontal sinus. 14. Bony bridge. 15. Upper lip. 16. Proc. alveolaris. (After Hirsch; Voorhees, *Medical Record*, Aug. 17, 1912.

mild adrenalin solution inserted through each nostril. Retracting the upper lip, an incision is made two to three centimeters long at the labiogingival border and carried down to the bone at the level of the anterior nasal spine. By blunt dissection on each side the margin of the bony nares and of the cartilaginous septum is exposed. The slight hemorrhage thus produced being once checked there is very little further bleeding, the balance of the operation being submucous. The mucosa is separated from the bony and cartilaginous septum on each side, giving extreme crowd the retractors to either side, thus flattening the turbinates instead of removing them, as is done by some operators; nevertheless if these are hypertrophied or seriously compromised they may require removal, which should have been done as a preliminary measure some days before the main attack and, preferably, under local anesthesia. After thus clearing the space a suitable bivalve speculum, with blades two centimeters wide and seven deep, is made to take the place of the retractors.

At least from this time on perfect illumination, by

FIG. 1061.

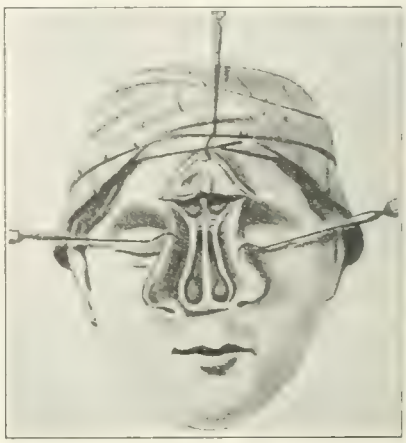

FIG. 1062.

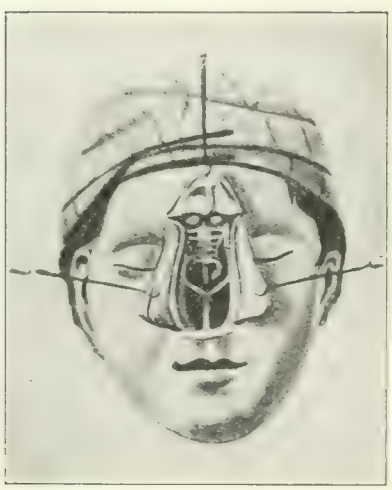

FIG. 1063.

FIG. 1064.

FIGS. 1061–1064.—Dialti's Method of Approach to the Hypophysis by Median Division of the Nose. (Dialti, Path. et Chir. de l'Hypophysis, Siena, 1910; Toupet, *Rev. de Chir.*, June, 1912.) 1061, Incision; 1062, the nose is opened by two lateral flaps, the frontal flap being raised; 1063, the septum is removed and the ethmoid cells are curetted; 1064, the hypophysis is exposed.

care to avoid puncture, and is carried back to the whole depth of the septum; deep smooth retractors, 1.8 wide and six centimeters long, are then inserted on each side and forcibly separated, thus making room for removal of a strip of this septum, including the vomer, the lower part of the vertical plate of the ethmoid, and all included cartilage. The anterior maxillary spine is then chiseled or cut away, any bleeding bone being treated with bone wax; save for blood from this source the operation is almost bloodless. Forcible dilators or plugs are now made to means of some form of headlight, is absolutely necessary, partly in order that the field may be kept absolutely dry. With these aids the sphenoidal attachment of the septum is identified, and the prow of the vomer removed. With a little experience the anterior wall of the sphenoidal cells is readily recognized, but one must keep low and follow the posterior margin of the vomer lest he enter the ethmoid rather than the sphenoidal cavity; this precaution is specially important because the former may be exceptionally large and the latter exceptionally small. (In one case

where Cushing met with this condition there was found, on autopsy, that very rare relic, a persistent craniopharyngeal canal.) After identification of the sphenoidal body the anterior and lower wall is bitten away with long-handled nasal rongeurs; thus the cells are opened and the mucous lining removed, after which inasmuch as it has no pia nor arachnoid, and does not lie in the subarachnoid space, the latter need not be opened, at least in most of these operations. A small knife hook is then used to seize and divide the capsule by a cross-incision of necessary length, and the pituitary is then drawn forward until its substance

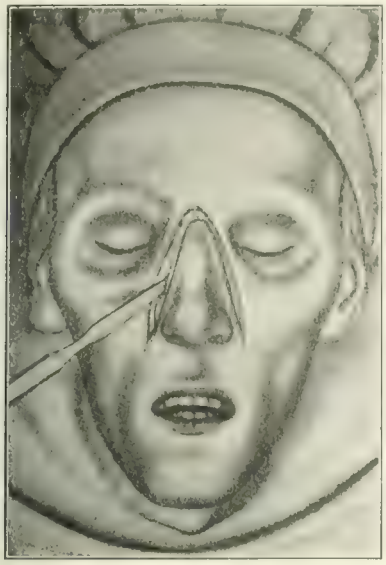

Fig. 1065.

Fig. 1066.

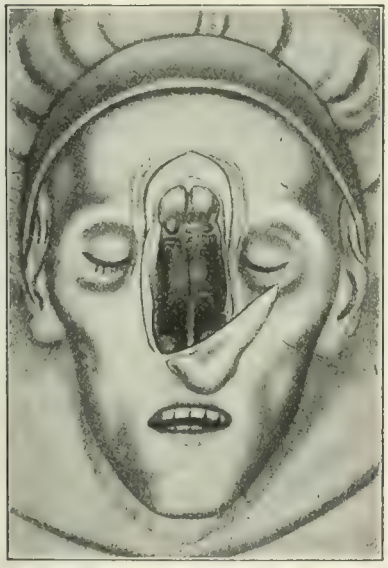

Fig. 1067.

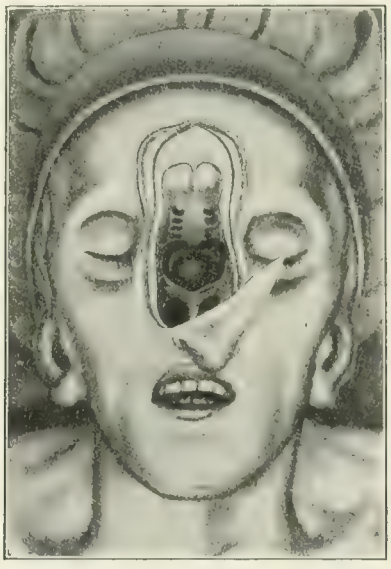

Fig. 1068.

Figs. 1065–1068.—Nasal Route of Approach to the Hypophysis. (Proust, *Journal de Chirurgie*, October, 1908.) 1065, Incision; 1066, rhinotomy, opening of the frontal sinus; 1067, the septum is removed, the ethmoidal cells are curetted; 1068, the sphenoidal sinus is opened and the sella turcica comes into view.

the sellar protrusion is usually revealed and easily recognized. With exposure thus made it should be compared with the findings of the radiogram, and each should corroborate the other.

The floor of the pituitary fossa is then exposed by chipping away the bone and the pituitary capsule. The pituitary lies enclosed within this capsule, but comes under observation. After this it remains only to meet whatever indication is afforded by its size, texture, etc. Its removal does not permit of a clean and total extirpation, but it has rather to be teased or torn away; thus it is never completely removed during operation on the living.

Frequent nostril packing, with tampons moistened

in hydrogen peroxide or in adrenalin solution, will enable the operator to work in a dry field; the speculum should not be withdrawn until oozing has ceased. A cigarette drain may be employed, being inserted through one naris, but even this is not always required. The nasal passages may be unavoidably opened, *i.e.* the mucosa punctured, especially at its perichondrial attachment at the anterior border of the cartilaginous septum.

An unusually small degree of shock or reaction attends these operations, and no mutilation or deformity of the face results therefrom, unless some anatomical anomaly, distortion, or diseased *anlage* offers unexpected complications. In the operation described by Hirsch removal of the turbinates was included; as seen above this may often be desirable. The most likely anatomical abnormality to be met with is the discrepancy between the average size of the sphenoidal and ethmoidal cells. On one occasion Cushing was compelled to leave a silver clip *in situ*, and to desist until another radiogram was taken, which revealed a complicated, dense mass of cancellous, sphenoidal body one centimeter thick; being thus orientated he was enabled, six days later, to discover and evacuate a cyst in the pituitary region.

Treatment of the Pituitary Mass.—Exposure alone is far from all that is called for, the main question being just how to deal with the actual lesion thus exposed. Thus a cyst may be evacuated, a struma partially extirpated, or a mere decompression may be all that is permitted, room being afforded for pressure in the downward and forward direction by removal of sphenoidal cells. One may even find an infrasellar tumor arising from a pituitary *rest*.

This operation, being practically extranasal and extradural, may be combined, if necessary, with a decompression operation upon either the temporal or frontal bone. Cushing has good reason for believing that by decompression not only are the optic nerves relieved from pressure, but even the brain itself from the encroachment of an advancing struma; also that the pituitary substance being thus uncovered is the more quickly affected by a short exposure to *x*-ray for therapeutic purposes, both through the nose, and from the lateral region. He would give this treatment, on alternate days, through a speculum, and over the temples. It is estimated that the actual therapeutic dose absorbable by the pituitary remains is not more than one-fifth of that absorbable by the skin.

A distended sella occupied by a struma is to be favorably regarded; these growths being relatively soft and non-vascular, and yielding easily to a sharp spoon, but when there is a large, interpeduncular tumor of sufficient size to produce serious neighborhood symptoms it cannot be removed in its entirety, and permits only of fragmentary extirpation. If what appears to be a true cyst is proved to contain cerebrospinal fluid then there is danger of infection, especially if the patient exhibit a postoperative rhinorrhea. In these cases urotropin is a remedy of the greatest value. Such cysts suggest a circumscribed, chronic arachnoiditis. The nature of the distinct tumors can usually be decided by aid of a frozen section, during the course of the operation, and upon the diagnosis may depend decision as to whether a lateral attack ought, also, to be made. Because many of these cases present a possibility of serious and diverse complications, Cushing advised that no specialist (rhinologist) should attempt the work alone.

If one adopt the lateral approach the right side is preferable since the right cerebral lobe is, perhaps, less important than the other. The posterior angle of the horseshoe flap called for in these cases should extend to the zygoma, which must be removed or at least divided, since one must approach from beneath the hemisphere, and a wide opening of the dura is important for the same reason; the osteoplastic flap, then, must be very wide. Operation upon a patient presenting greatly increased intracranial tension will be much more difficult than the same procedure rehearsed upon the cadaver. Even a double flap (bilateral), with division of the tentorium, may be required. In such case the third nerve and the carotid artery may be exposed, the latter often enveloped in the tissue of a large struma.

The possibility of *transplantation* after removal of a considerable portion of the hypophysis will depend upon the future developments of neurosurgery. Cushing's sole effort, in which he took material from the dead body of a new-born child, was encouraging but not finally successful.

So far as the mortality after operating by this method is concerned Cushing lost four out of twenty-nine cases, *i.e.* fourteen per cent.; three of the four deaths occurring in patients already far advanced in the disease process.

Modifications of the methods of attack have been proposed by numerous surgeons and some of them may, perhaps, be adapted to certain cases presenting peculiarities of their own; thus, as has been already mentioned, Krause suggested an approach from the front, by raising a very large horseshoe flap of frontal bone upon the side selected, and then elevating both the dura and the lobe together. On reaching the anterior clinoid process and the edge of the great wing of the sphenoid he made a transverse incision in the dura, between the optic nerve sheaths, about one-half centimeter above the bony floor of the frontal fossa, thus exposing the chiasm with the pituitary just beneath. He recommended especially to use a hook-shaped knife so as to avoid the blood-vessels beneath and below the dural incision, and he insisted that it was possible, by this incision, to remove the anterior part of the hypophysis.

Kiliani extended this procedure by resecting nearly all of the frontal bone, after double ligation of the longitudinal sinus, making a transverse section of the dura lining the skull, and lifting up the brain exactly as is done in an autopsy.

McArthur has described, perhaps, the most practicable method from the front, in brief as follows: An incision is made over the right, shaved eyelid, from the inner to the outer angles, the supraorbital vessels are tied, but the nerve is spared. A vertical incision is made in the midfrontal line or furrow, some four centimeters upward, the periosteum is raised with the skin and stripped from the bone, while the periosteum is also stripped from the orbital roof, and the orbital contents are displaced downward. The bone is divided with chisel directly from the lower end of the longitudinal sinus, and the inner end of the frontal sinus upward, by a curved incision terminating at the external angular process. Here a sharp osteotome, with edge one-half inch wide, is directed upward and inward from the outer wall of the frontal sinus, and, then, at the external angle it is likewise divided by directing the instrument horizontally inward. With two or three suitable elevators the frontal fragment is then carefully detached, along with the anterior half of the orbital roof; this fragment being at once placed in warm sterile salt solution. The remainder of the orbital roof is then bitten away, with suitable rongeurs, back to the optic foramen, without injuring the dura, the frontal lobe with its dura being lifted out of the way. After reaching the anterior clinoids the edge of the wing of the sphenoid is then recognized, either with the finger or the hook, at a point where the bone shelves off to the sella; then between the two clinoids the two- or three-centimeter incision of the dura is made with the hook-shaped knife, about one-half of one centimeter above the level of the anterior fossa, thus avoiding the small, transverse, venous sinus which occupies a groove between the optic foramina

which, until recently, was wrongly regarded as being occupied by the optic chiasm. After this procedure the nerves, with their chiasm, and any abnormal pituitary enlargement should be exposed. The special dural cavity of the pituitary may require tearing or division before the body rises to view. Up to the point of incising the dura no really important structure is injured by this operation. After treating the pituitary lesion as may seem wise, according to its nature, the large bony fragment is replaced, one or two thin drains are inserted, and the periosteum is stitched, the peculiar shape of the fragment aiding its reposition.[4]

Chiari has recently recommended a more distinct orbital approach by removing its internal wall, thus gaining access to the posterior nares without disturbing, anteriorly, the bony tissues. His incision also is made along the line where the eyebrow has been shaved.

To prevent otherwise unavoidable destruction of any part of the pituitary, which may be desirable to preserve, is to display judgment in the route of attack.[5] When the anterior lobe is affected then the nasal method is usually by far the best. When one contemplates attacking the posterior lobe then the lateral route is probably the only one permitting it.

Roswell Park.
Edgar R. McGuire.

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Brain, Syphilis of the.—The subject of brain syphilis is a broad one, and furthermore it is one that escapes all attempts at narrow descriptive control. The clinical forms of syphilis of the brain, as well as of the nervous system, in general, are largely abstractions. The underlying pathological processes are either meningeal, arterial, or infiltrative, that is gummatous, and these processes may either exist alone or in various combinations, so that an extremely variable, complex, and confusing series of clinical syndromes may arise, depending upon the interrelationship of the pathological trends and the anatomical paths or centers implicated or destroyed.

So far as the therapy of syphilis of the brain is concerned, these confusing clinical pictures are fortunately of minor interest. Yet, it is desirable to obtain as clear a clinical grasp of a cerebral syphilis as possible, for such an insight is often extremely valuable from the standpoint of therapy. This is seen particularly when one comes to treat certain forms of cerebral syphilis which clinically resemble certain forms of general paresis. It will be recalled that a more or less widespread nihilistic attitude obtains with reference to the possibility of obtaining relief in the treatment of paresis. Such an attitude toward this particular therapeutic problem unfortunately is capable of being extended to a paresis-like picture, which on close analysis will be found to be a cerebral syphilis of a secondary or curable character. This is but one illustration of a series of situations which emphasize the need for clearer clinical differentiation. It is for this reason largely that a more or less arbitrary series of types has been created by the students of the problems of cerebral syphilis.

Following a classification which the writer has followed in "Treatment of Nervous and Mental Disorders" vol. ii. (Lea and Febiger, 1913), the subject will be discussed here under the following clinical forms: (1) Syphilis of the cranial bones; (2) syphilis of the basal meninges; (3) syphilis of the convexity; (4) cerebral syphilis, arterial types; (5) meningoencephalitis, paretic and taboparetic types; (6) syphilitic psychoses; (7) hereditary syphilis of the brain.

In a discussion of syphilis of the nervous system, the forms of syphilis of the spinal cord which accompany that of the brain, might properly be included, but are excluded from this article by reason of its title.

1. Syphilis of the Cranial Bones.—Only those which cause symptoms of brain involvement are mentioned here. In the works of the early clinicians of the middle of the sixteenth century, syphilis of the cranial bones was very frequently described, and it would seem that throughout the sixteenth, seventeenth, and eighteenth centuries brain involvement through extension of gummata of the dura and of the bones was more frequent than at the present time. This diminution in cases observed is probably due to the better treatment to which syphilis is now subjected.

In discussing syphilis of the bones of the skull, gummata are practically the only pathological forms of interest. They are usually circumscribed, and when large enough to cause symptoms, give rise to the picture of a tumor of the brain. The exact trend of

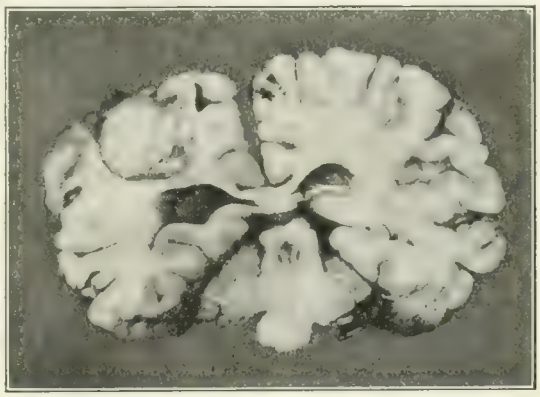

Fig. 1069.—Gumma of Dura, Causing Symptoms of Brain Tumor and Epilepsy. (Larkin.)

symptoms depends largely upon the location. Not infrequently they give rise to epileptiform convulsions. When impinging upon the motor areas they have been known to give rise to various forms of monoplegia, hemiplegia, aphasia, or even sensory eye signs. The gummata of the frontal region which protrude into the frontal lobes may give rise to a psychotic picture, at times accompanied by "Witzelsucht."

The general symptoms of brain tumor, such as headache, nausea, vomiting, sleeplessness, and choked disc are to be expected. In the autopsy records of Mott, Nonne, Oppenheim, and others, one is struck with the frequency with which these cases are treated as epileptics. Not infrequently cranial bone gummata involve the base with caries, the upper vertebræ often affording complications. Here stiffness and rigidity of the neck are not infrequent signs.

It is important to bear in mind that many of these gummata are best attacked by surgical means. It is futile to attempt to get rid of them by antisyphilitic measures, especially when they are large and dense.

2. Syphilitic Meningitis of the Base.—This is a very frequent form of cerebral syphilis. The optic chiasm is involved quite often in the very early stages of the meningitis. Spreading in all directions from here, the thickening of the meninges and the infiltration of the gummatous growth brings about a very complicated symptomatology. The gummatous masses invade the brain structure, grow about the emerging and entering cranial nerves, and may even

involve the bones of the base, and the upper cervical vertebræ. The diffuse type making up a gummatous meningoencephalitis is most frequent, but at times a syphilis of the base will consist of an isolated vascular disease, or of circumscribed gummata, or possibly even simpler manifestations of the disease, giving rise to very simple pictures, such as a primary optic neuritis, or paralysis of a single cranial nerve, or a mild headache and rigidity of the neck.

The general picture, however, is apt to be more complex. In its initial phases headache, increasing stupidity, increasing emotional apathy, forgetfulness, negligence of personal appearance or business engagements create the impression that a paretic process is in course of development, but as the infiltrating or gummatous growths increase the cranial nerves are involved, thus introducing certain variants which permit a diagnosis. Headache is a frequent sign, is often boring or stabbing in nature, the head

Fig. 1070.—Cerebral Syphilis of Base. External rectus palsy.

showing tenderness on percussion, especially over the occiput. Optic nerve changes develop in from twenty to forty per cent. of the cases, one eye or the other showing choked disc or atrophy. The sixth nerve is most frequently involved. As it has a long pathway on the base of the skull it is most likely to be caught in the gummatous infiltration. Internal strabismus is thus a frequent sign. The third nerve in some of its branches is also often implicated. Ptosis in one eye develops early, then rectus palsies follow, one pupil commences to dilate, or becomes irregular, then loss of pupillary reflex shows with final development of an Argyll-Robertson syndrome. This is apt to be incomplete, and not as in those forms of cerebral syphilis of a more ideal paretic, or taboparetic nature.

Painful flashes in the side of the face, changes in sensibility, point to implication of the trigeminus; facial palsy may result in others. The IX., X., XI., and XII. nerves may be caught in the syphilitic exudate, with changes in the respiration, irregular heart action, hemiatrophy of the tongue, etc., as their characteristic symptoms. The mental picture, as

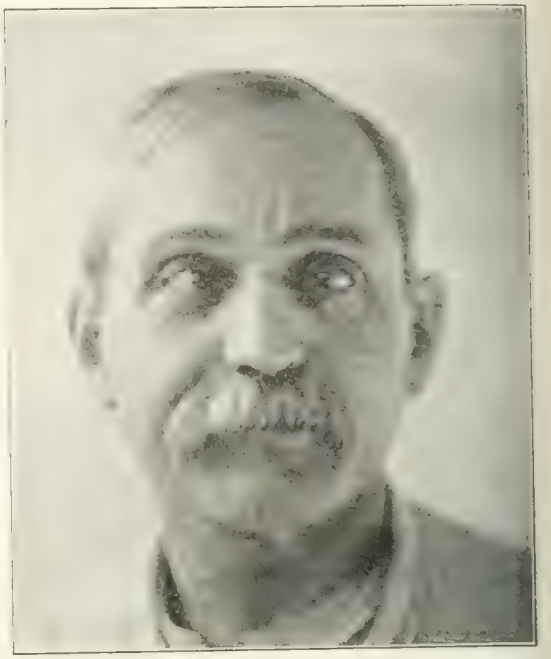

Fig. 1071.—Cerebral Syphilis of Base. External rectus and superior rectus palsies.

Fig. 1072.—Cerebral Syphilis. Fourth nerve palsy.

already outlined, is striking. There is a half dull, apathetic psychosis that not infrequently suddenly gets worse, with coma or unconsciousness, with

periods of acute confusion, possibly of violent delirium. The marked variability in the dulness, apathy, or coma is very characteristic of basal syphilis. Certain patients show a mild delirium, others are fairly violent, resembling an acute attack of meningitis, or a manic depressive psychosis. Many of

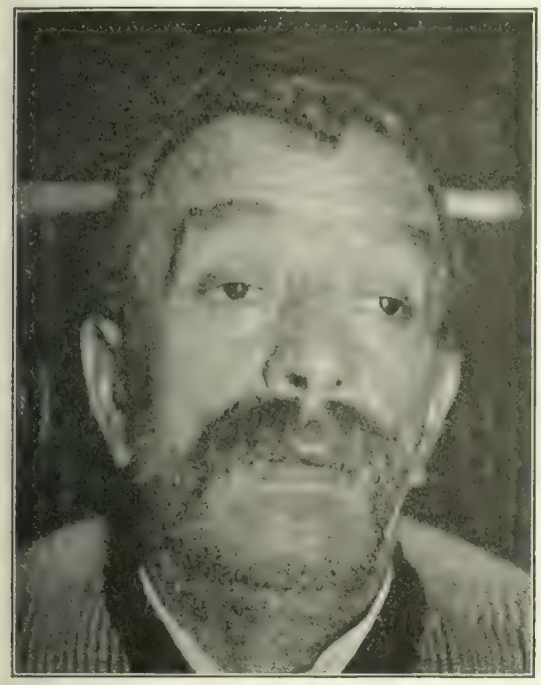

Fig. 1073.—Cerebral Syphilis. Palsy of III. and VI. nerves. (Sharp.)

these cases suddenly clear up, apparently from no reason whatever. This is a not infrequent situation in these basal syphilitic cases. At times the patients show depressed phases, again they are confused; still others would pass for dements, while others again would be diagnosed as manic depressives. A few show persecutory notions, and in the language of the descriptive psychiatry of ten or fifteen years ago these would be called by the names already indicated. Present day psychiatry regards them solely as kaleidoscopic mental picture variations of one disease, namely syphilis. This point of view has come about through careful studies, and through the gradual extension of knowledge of the cytology and serology of the blood and cerebrospinal fluid. Naturally this point of view aids to a much more enlightened therapy, for one does not attempt a treatment of mania, or dementia, or melancholia which are names solely, when after all one should treat syphilis which is a definite affair.

3. Syphilitic Meningitis of the Convexity.—It is largely through a variety of the trend of the symptoms, rather than from any fundamental pathological difference that this subdivision is made. In many individuals syphilitic meningitis of the base is accompanied by one of the convexity as well, and practically all cases of syphilitic convexity meningitis show some signs of syphilis elsewhere. The only question here is of a greater predominance of localization of pathological processes in the convexity rather than in the base. Just why such localizing factors should be at work is not altogether apparent. Sometimes it is due to a blow, again possibly such a localization may be determined by the presence of local minor injuries. Here marked localization may be present, or the process may be a diffuse one; it may limit itself solely to the meninges, or there may be an underlying encephalitis. Gummatous infiltrates or nodules may predominate.

Headache is usually present, often paroxysmal, at times migrainous in character, frequently increasing in nocturnal severity. Local pains on percussion, and tenderness are frequently found. Symptoms of general brain pressure are apt to be less here than in basal meningitis, but there may be nausea, vomiting, and giddiness. The optic nerve changes are less liable to be found.

Epileptiform convulsions are not infrequent, and simply indicate the localization of the process. When the attacks are Jacksonian in type, the presence of an isolated gumma may be suspected.

Aphasic attacks, especially of motor aphasia of the Broca variety, are also to be reckoned among the isolated symptoms, and speech difficulties which do not develop into true aphasias are not infrequent. Monoplegias or hemiplegias may develop, with or without sensory disturbances, hemianesthesia, astereognosis, etc.

When the layers of the cortex are involved as well as the meninges, one sees the gradual development of a mental picture closely resembling that of paresis, in fact, in a certain percentage of cases a clinical differentiation is impossible. Here one finds a slowly increasing apathy, forgetfulness, indifference, and all the signs characteristic of general paresis (*q.v.*). The application of Nonne's four reaction tests gives valua-

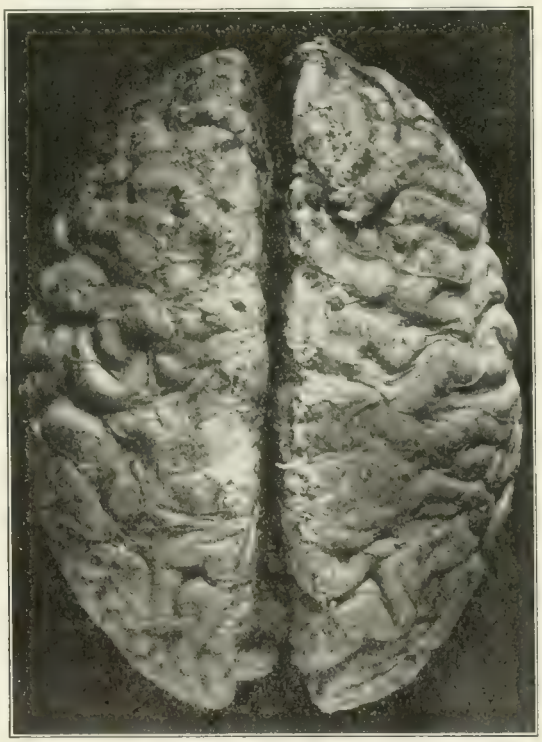

Fig. 1074.—Syphilitic Thickening of the Meninges. Epileptiform convulsions.

ble insight into the process, for in paresis, as a rule, the four reactions are all positive, whereas in cerebral syphilis of this type the cerebrospinal fluid is not apt to show a positive Wassermann reaction, whereas the blood is positive, there is usually a high grade of lymphocytes, and there is a positive globulin

Fig. 1075.—Syphilitic Leptomeningitis, Hemorrhage, Softening. Meningoencephalitis.

Fig. 1076.—Cerebral Gumma in Brain Substance. Epileptic. (Lafora.)

reaction. This four reaction test, however, is not absolute. It cannot be entered into here at greater length.

4. Cerebral Syphilis. Arterial Types.—Here one distinguishes two very pronounced types, although intermediate forms are the rule. One speaks of (*a*) cerebral syphilis of the smaller vessels, Heubner type, or (*b*) cerebral syphilis involving the larger vessels with embolism, thrombosis, or even hemorrhage, giving rise to the classical hemiplegias. In the former type, that of cerebral syphilis of the smaller vessels, one has presented the classical picture, in the mild grades, of persistent headaches with slight mental changes; in the severer grades, the picture of a general paresis. The patients show various forms of acute convulsive attacks, comatose periods due to softenings in this or that portion of the cerebral cortex, the picture often resembling that of a pronounced senile dementia or a pronounced paresis, with aphasias, word blindness, astereognosis, monoplegias, etc.

There is a great multiplicity in the syndromes present in cerebral syphilis of this type. One characteristic feature is that of the remissions, which are also so frequent in paresis.

In cerebral syphilis of the larger vessels, we found the characteristic apoplectiform results that mark hemiplegias or hemianesthesias, thalamic syndromes, etc., which are discussed in this work under the head of *Hemiplegia*.

All of these forms of syphilis are characterized

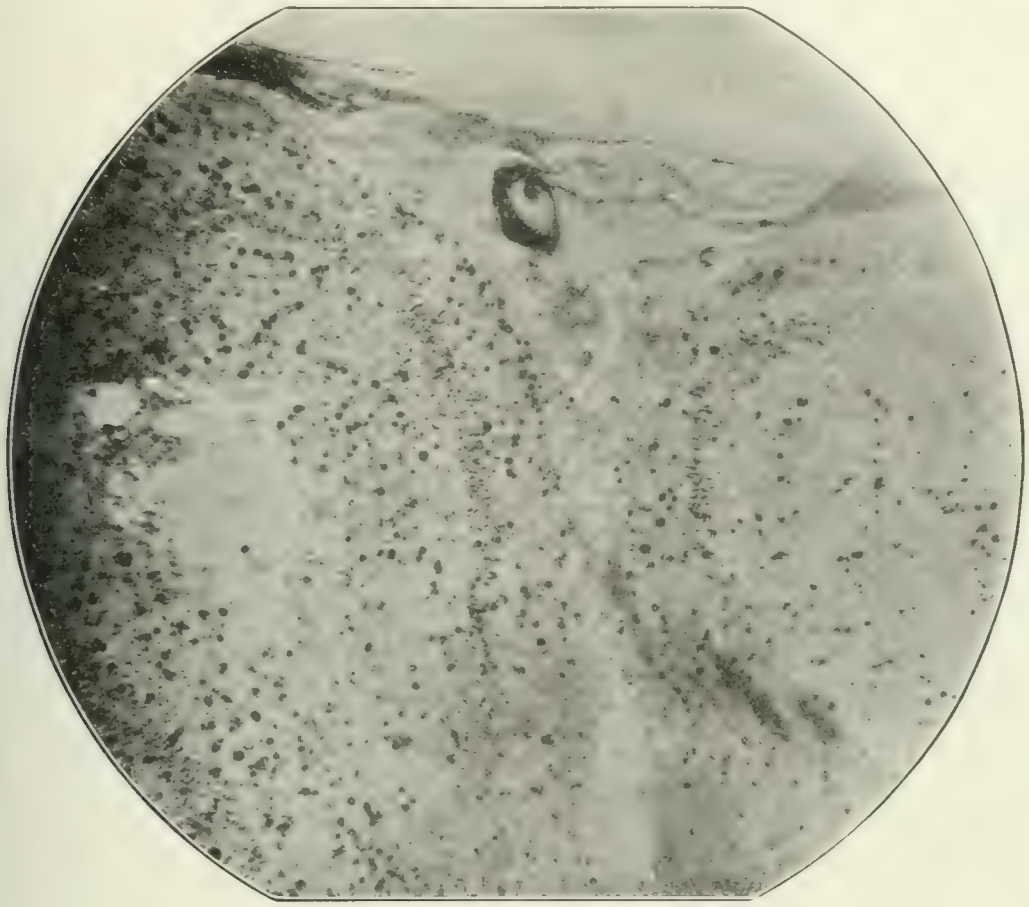

Fig. 1077.—Cerebral Syphilis. Arterial type with softening.

more or less by the comparatively rapid appearance of the symptoms following infection. Basal syphilis, convexity syphilis, syphilis of the small arteries, or hemiplegic syndromes, due to involvement of the larger vessels, thrombosis, etc., may come on as early

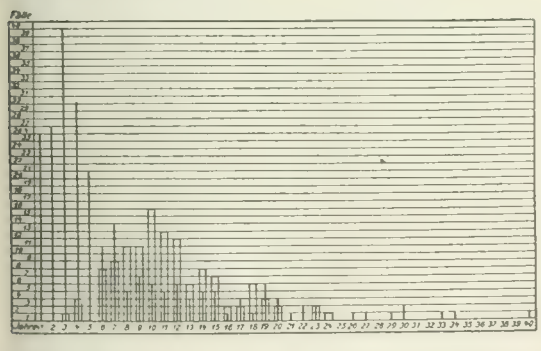

Fig. 1078.—Length of Time after Infection of Appearance of Cerebral Syphilis (single line) and of Paresis or Later Syphilis (double line) of Brain. (Kraepelin.)

as from three to six months after an initial infection. The average time, however, varies from one to three years, the maximum possibly expressing itself about the third year, whereas, as is well known from the studies of Fournier, Kraepelin, Junius, Arndt, and others, paresis is apt to come on much later, the maximum paretic development showing about the tenth year. Still, cerebral syphilis, in certain of the forms here described, may occur many years after infection, certain cases being reported as late as forty years after infection. This, however, is a marked exception.

Treatment.—The treatment of these forms may be discussed in one paragraph, as the objects are practically the same, namely, to kill the syphilis organism as rapidly as possible, and to reduce the effects of the pressure symptoms due to the gummatous or inflammatory exudates. This is not the place to discuss prevention. Individual prophylaxis also is out of place here.

The treatment is very satisfactory, especially if the diagnosis is made early, and the patient has never received much treatment, but in old long-standing cases, which have been much treated, and yet seem to progress in spite of treatment, the outlook is not very hopeful. This latter result is often due, we feel, to insufficient and half-hearted therapy. Cerebral syphilis is usually accompanied by spirochetes, and the object is to poison them as rapidly as possible. This can be done by arsenic, by mercury, and by the iodides, but these remedies have a very definite variation in their spirochetal toxic properties. Arsenic is the most active, mercury next, while the toxic action of the iodides, although positive, is very slight. The treatment of cerebral syphilis should be most energetic, because small lesions may involve very important areas and result in great deprivation to the patient. The nervous and mental structures

are of the greatest importance to the individual in his struggle for existence, therefore, syphilis of the brain is always an extremely dangerous disease. A complete sterilization is desirable, but this is often difficult to bring about, especially in nervous tissues, for reasons as yet not competely understood.

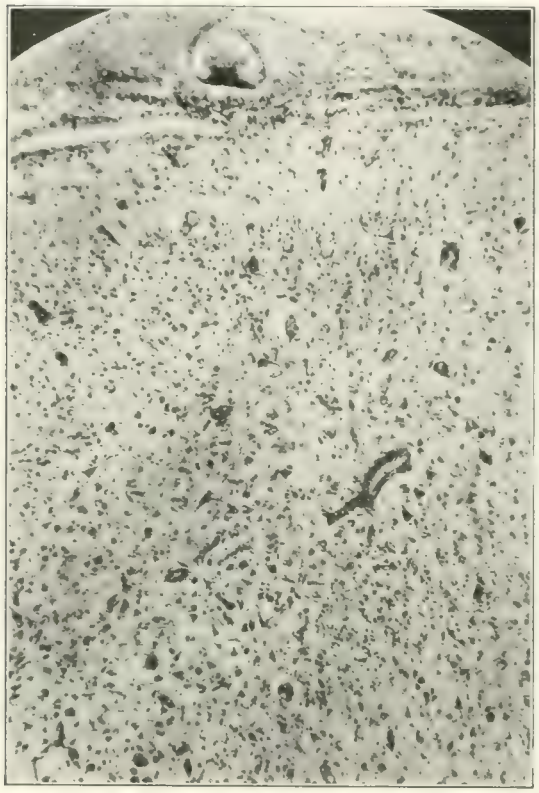

Fig. 1079.—Cerebral Syphilis, Paretic Type.

As has been said, cerebral syphilis may present a positive cerebral spinal fluid Wassermann without a positive blood Wassermann. Hence, a negative Wassermann should not deter one if the diagnosis is fairly well established. In fact, an active antisyphilitic treatment, as, for instance, by salvarsan, may suddenly bring about a change in the Wassermann reaction, showing that latent spirochetes have been stirred up.

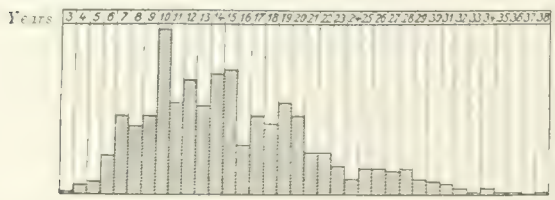

Fig. 1080.—Length of Time after Infection of Appearance of Clinical Signs of Paresis. (Kraepelin.)

Space is not available for a complete discussion of the treatment of cerebral syphilis, but it would seem that the trend of modern opinion is to attack it very actively. The attack, however, should be begun with a certain amount of moderation. The following general suggestions are given:

Combined salvarsan and mercury treatment has seemed to give the best results. The patient should be given a dose of calomel by injection on the first day, to be followed by a similar dose on the third day. On the fifth day he should be given 0.6 gram

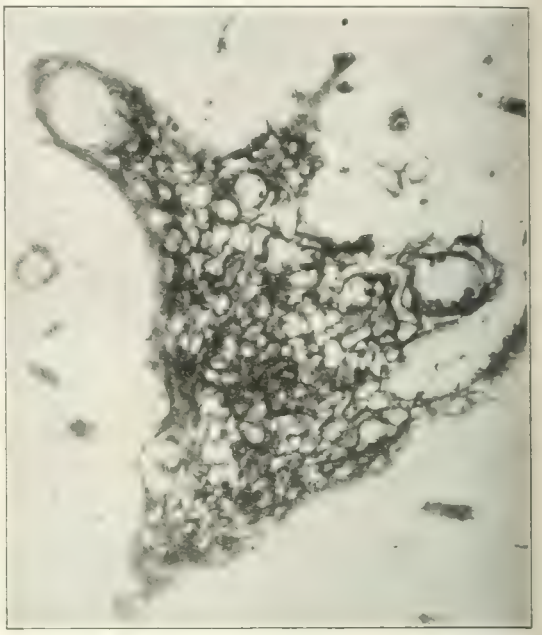

Fig. 1081.—Lymphatic Spaces with Replacement Tissue in Paresis. Possibly one cause why toxic substances cannot get in touch with spirochetes and kill them.

of salvarsan or neosalvarsan by the intravenous method. The seventh and ninth days, intramuscular injections of calomel, the eleventh day another dose of salvarsan, the thirteenth and fifteenth days, two injections of calomel, the seventeenth another of

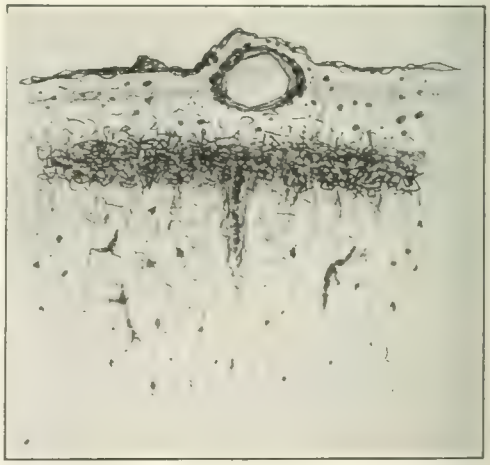

Fig. 1082.—Proliferation of Glia in Paresis. (Lafora.)

salvarsan, and this should be continued for at least six weeks, unless specific indications of mercurial poisoning arise which render it necessary to cut down the amount of calomel. In this case a less active form of mercury can be given, such as salicylate

or cyanide, but at least five grams of salvarsan should be used in the therapy. To give one, or two, or three doses of salvarsan invites failure, and, we are tempted to believe from more recent studies, tends to permit the development of the more feared metasyphilitic processes of paresis and taboparesis. This is an outline of an energetic antisyphilitic therapy.

For years it has been the custom to praise the use of mercurial inunctions in the treatment of cerebral syphilis, and clinical experience seems to show that they are of much value, but similar experience seems also to indicate that thus far the inunction treatment has not been sufficiently prophylactic with reference to the moe severe forms of cerebral syphilis. It is hoped that the combined method of mercury and salvarsan will provide this prophylaxis. Mercurial injections may be substituted for the combined method, or for the method of inunction, but these do not seem to be as radical as the method already outlined. In the later stages of the treatment, daily doses of from 30 to 40 grains of potassium iodide may be given for from four to six weeks.

Fig. 1083.—Infiltration about Vessels and Lymphatics in Paresis Possibly barriers to therapy.

After such a complete "cure" has been instituted, the patient should be allowed to rest untreated for about three or four months. A Wassermann should be then taken and a cerebrospinal-fluid examination made and if the biological and cytological reactions indicate that the spirochetes are still active, or have renewed their activity, the patient should be put through a similar cure. This can be repeated again after an interval of five or six months. Ideally, one can check the effect of the treatment by reason of the Wassermann reaction; practically, however, this seems to be unnecessary, if not utopian.

5. Cerebral Syphilis of the Paretic and Taboparetic Type.—See *Paresis, General.*

6. Neuroses and Psychoses.—These will be discussed under the head of *Psychoses, Syphilitic.*

7. Hereditary Syphilis.—This is of tremendous importance in its effects upon the nervous system. Statistical studies show that at least 66 per cent. of the children of syphilitic parents—without counting the immense number of abortions and of still-born children—show the taint in some form. Fournier places the ratio as high as 98 per cent., and says that 68.5 per cent. of the children die. Hochsinger reports that to seventy families, out of a group of seventy-two, in which there was paternal syphilis alone, only thirty-one healthy children were born, and these in all save four instances were the latest born. Of the remaining 276, 110 were still-born, 166 were syphilitic.

Mott, Mendel, and others tell the same tale of the children of paretics and tabetics—either no children, or many abortions, many dead children, and a few living of whose fate there is as yet no certainty. Probably more than half are doomed to some disease or disorder of the nervous system.

Apparently the commonest effect of hereditary infection is the reduction of resistance in the body, and of the powers for full development, in both the general body and nervous tissues. In a manner analogous to the influence of alcohol on the germ cell, syphilis diminishes the vital energy of the plasm prior to conjugation, causing pathological variations in nervous structures, just as it can transmit the disease through

Fig. 1084.—Hematoma of Ear in Excited Patient with a Syphilitic Psychosis.

the germ cell. In the result, Fournier's classical formula of abortion, dead child, early death, living healthy child, might be amended to read complete sterility, miscarriage, abortion, still-births, children dying in infancy or convulsions, marasmus, meningitis, hydrocephalus, comparatively healthy children who will probably in later life develop late hereditary syphilis. On this point, a study of Mott's family trees will prove valuable and instructive.

On the question of the mode of transmission much light has been thrown by late serological studies, particularly those of Plaut. (See "The Wassermann Serodiagnosis of Syphilis in its Relation to Psychiatry,"—Translated by Jelliffe and Casamajor, Nervous and Mental Disease Monograph Series, No. 5, New York.)

Space will not permit us to catalogue the general signs of hereditary syphilis, and for general information as to its effect upon the nervous system, reference may be made to Hochsinger's studies (Ergebnisse d. Innere Med., 1910, *Wien. klin. Woch.*, 1911). He held 208 children of syphilitic parents under observa-

tion for five years, and states that in that time forty-three per cent. showed some disease of the nervous system.

Whether syphilis can be transmitted to the third generation has been a much discussed question. Very suggestive material has of late years pointed to the probability that this occurs. Mott of London has shown some very pertinent hereditary material before the Royal Society and which is reported in their Transactions for 1912.

The logic of this is clear in the light of the recent observations made by Levaditi, Bab, and others that *Treponema pallidum* may be found in the ovum, and in an apparently resting stage, similar to the resting stages known for other flagellate protozoa, closely allied to the organism causing syphilis. Jonathan Hutchinson is sceptical as to this, but he was also sceptical as to juvenile tabes and paresis—possibly in medicine ultra conservatism is psychologically an interesting individual idiosyncrasy rather than a sound pragmatic instinct.

The necessity for the use of all available biological tests in the matter of congenital syphilis is very great, because statistics and opinions uncontrolled by them, and unsupported save by clinical observations are not only insecure and insufficient approximations, but, if relied upon in the negative, may retard the progress of thought, and delay the relief of sick humanity.

Without losing sight of the immense importance, and the striking and ofttimes grewsome character of the congenital cases which appear in later life, if the physician would place himself in the right attitude toward the therapeutics of this disease, he must focus his attention on the preponderating number of miscarriages, still-births, and early syphilitic births. The psychological control, the so-called ethical attitude toward sexual freedom as one of the burning factors in the present cultural struggle for more efficient sexual adaptation is a problem too large to be entered into here.

Congenital syphilis may occur at any age. It is not infrequently a cause of death of the fetus, and gives rise to a great variety of intrauterine cerebral diseases which, if the child is born alive result either in early death, or in early disease, or the later development of various congenital syphilitic manifestations, chief of which are idiocy, imbecility, feeble-mindedness, epilepsy, deafness, optic atrophy, tabes, and paresis.

The symptoms are a duplication of those found in the adult types, and the clinical picture is apt to be conglomerate and difficult of analysis. Endarteritis, leptomeningitis, pachymeningitis, gummata, diffuse degenerative changes in the cells of the spinal cord, in the basal ganglia, or in the cortex, all are found and in varying combinations. Consideration will be given here to those trends which are sufficiently accentuated to permit of definite nosological terminology.

Hydrocephalus.—This condition, resultant from congenital syphilis, has been suspected for over two centuries, and was so reported by Haase, Cruveilhier, Von Rosen, and Virchow in the last century. In its congenital form, it arises chiefly from syphilitic disease of the cerebrospinal fluid producing structures—choroid, ependyma—or from definite obstructive factors in the cerebral foramina, gummata, vascular swelling obstructing the iter, etc. It frequently follows after congenital syphilis, and is without doubt much more frequent than is commonly realized. Hochsinger cites ten per cent. of hydrocephalus in 362 cases of congenital syphilis. In the series recorded by him, and which gives a fairly average review of the whole situation, the hydrocephalus was sometimes fetal, and usually began from the third to the eleventh month after birth. Up to the time that his report was written absence of nervous symptoms were noted in only eleven of the 362 individuals. In the others the phenomena ranged through restlessness, sleeplessness, chronic vomiting, convulsions, contractures, nystagmus, and feeble-mindedness.

The ordinary clinical picture is that of an infant of from three to six months old who, apparently without reason, or it may be a slight blow on the head, or a trivial gastrointestinal or bronchial disturbance, develops within a few days grave cerebral disturbances. The child is very irritable and sleepless, screaming and kicking. The head is usually drawn back, the eyes and the fontanelles are apt to bulge. There is

Fig. 1085.—Hydrocephalus with Atrophy of the Entire Pallium. Clinically epilepuform convulsions, feeble-mindness, motor defects. (Craig Colony.)

frequent vomiting, and there are signs of oculomotor involvement. Internal strabismus resulting from paresis of the external rectus is a usual sign which is frequently preceded by or accompanied by nystagmus and irregular pupils—often not responding to light. The child cries and struggles, and ofttimes with spasmodic or convulsive movements of the arms it seems to try to brush away the source of the pain which is present in the head; pulling the hair, grasping and rolling the head. It is sometimes possible to demonstrate spasticity, rigidity, and other signs of intracerebral pressure. As a rule there is no heightening of temperature, and such signs of epidemic cerebrospinal meningitis as herpes, and flushed and spotted skin are absent.

There is great difficulty in the diagnosis of all these infantile meningeal disturbances.

Feeble-mindedness.—The very large rôle played by syphilis in the production of mental defectives has been realized only of late years. Early statistics are comparatively worthless. Even recent works—particularly English studies, excepting always those of Mott and his coworkers—show a tendency to mini-

mize its importance, showing an unconscious desire to suppress disagreeable truths.

The intimate correlation between syphilis and feeble-mindedness was first definitely brought out by Fournier, the conclusions being forced upon him by his clinical observations on parasyphilis. Following him the early English, German, and American figures varied from 0.01 to 17 per cent., but since the introduction of exact serological investigation they have gone as high as forty per cent.

Feeble-mindedness is thus shown to be the result of more than one cause, but as we are not here dealing with it in its larger aspects we limit ourselves to that of purely syphilitic origin.

This may date from intrauterine life, but rarely. Children who are infected thus early usually die, and Plaut (*loc. cit.*) is authority for the statement that so far as syphilis is concerned, feeble-mindedness may be regarded as the result of extrauterine syphilitic disease, incurred in infancy. In some there are signs of an acute brain disease; some cases of recovered hydrocephalus later show signs of havoc in their inability to develop normally. Many simply fail to develop. There are many recorded observations of mental defect of very gradual development, without convulsions or fever, or other signs of organic disease, arriving at a definite termination and leaving behind as a result entirely stationary, perhaps even improvable, idiots or imbeciles.

The Wassermann reaction is frequently shown in Fournier's "enfants arrièrés," the type of hereditary syphilitic children described as unintelligent, simple, silly, limited children, always behind.

Nonne's reported cases of general irritable weakness of the nervous system, and the researches of others, convince one that a less marked grade of mental defect, along more restricted or special lines, is closely allied with this broad group as a result of congenital syphilis. The patients are highly excitable, show extreme nervousness and moodiness, suffer from headaches, irregularities of appetite, and sudden fits of passion—without other epileptiform analogies. Mercury and the iodides worked wonders for Nonne's cases.

Many so-called psychopathic children are also to be included in this broad group of congenital syphilitics. These children are intellectually bright, but show marked ethical defects, and one can conceive of the mental defect in terms of limited cortical control to the affective response of the sexuality, and to the nutritional instincts. They want, and indulge their wants, without taking the circuitous routes devised by cultural standards. Anatomically one can posit, on the basis of the syphilitic poisoning, a defect or destruction of certain corticocortical association areas.

SMITH ELY JELLIFFE.

Brain, Topography of the.—See *Cranio-encephalic Topography.*

Brain, Tumors of the.—Tumor formation within the cranial cavity is not a very rare condition as it comprises about two per cent. of all cases of disease of the nervous system. It is very rare in early infancy but not infrequent in children. The greatest number of cases, however, occur between the ages of twenty to forty years. Old age is comparatively exempt.

VARIETIES.—*Gliomata* are among the most frequent of the tumors of the central nervous system. They develop from the gray matter of the cerebral cortex, cerebellum, basal ganglia, or floor of the ventricle although they may develop in the white matter or even in the tissue of a cranial nerve, a glioma of the optic nerve having been described by Chiara. They are usually single tumors, growing with moderate rapidity and not encapsulated, infiltrating the normal brain tissue so that a microscopic examination may show them to be considerably larger than they appear on gross examination. Sometimes the gliomatous infiltration of a part of the brain gives rise to the appearance of simple hypertrophy of the brain as has been pointed out by Marburg. Their appearance is grayish, or reddish-gray from excessive vascularization, and they resemble normal brain tissue very closely. They are soft to the feel and may contain cavities in the center due to degenerative changes. Microscopic examination shows that the tumor is composed of neuroglia, cells and fibers, which can be demonstrated as such by special staining methods. The nuclei frequently show mitotic figures. Nerve fibers, medullated and non-medullated, frequently pass through these tumors unchanged (Byrnes).

The term gliosarcoma is sometimes used to indicate unusual forms of either gliomata or sarcomata. Ependymoma is a term applied to tumors developing from the ependyma of the ventricle. They may take on the appearance of sarcoma or carcinoma.

Sarcomata of the brain are almost as frequent as gliomata. They develop from the meninges, blood-vessel walls, nerve sheaths, or other places where connective-tissue elements are found. Primary sarcomata usually develop as single tumors, grow with fair rapidity and frequently attain large dimensions. They are of varying consistency but are usually more dense than brain tissue and are almost always encapsulated or otherwise sharply demarcated from the cerebral substance. They are often highly vascular (angiosarcoma). All varieties (large or small round cell, or spindle cell) can occur, as in other parts of the body. Various mixed types occur, such as fibrosarcoma, myxosarcoma, etc. Multiple sarcomata are not rare but ordinarily cerebral sarcoma is more benign and shows less tendency to metastasis than sarcoma of other parts of the body. Sarcoma can take on the character of a diffuse process involving the meninges, only recognizable on microscopic examination. A sarcomatous neuritis of the cranial nerves has been described by Darkschewitz.

Endothelioma is a term applied to tumors developing from the endothelium lining the blood-vessels or the lymph spaces of the meninges but they are especially liable to develop in the latter situation. They are slow-growing tumors generally favorable for operation on account of their situation and the fact that they are usually well encapsulated and can be easily shelled out. They, however, give rise to frequent metastasis, often recur after removal, and are sometimes widely diffused in the meninges or follow the blood-vessels. Those arising from the blood-vessels are sometimes spoken of as perithelioma. The endothelial cells are frequently arranged in nests and whorls and sometimes contain hyaline bodies. Cylindroma is a name applied to some of these tumors with marked hyaline change. Perithelioma may be metastatic from the adrenal, thyroid, etc.

Psammomata are tumors composed wholly or largely of concretions of calcium carbonate. Such concretions may be present in tumors of various sorts—sarcoma, fibroma, etc.—but are most common in endotheliomata developing from the dura. Tumors of the pineal gland and choroid plexus are usually of this variety and I have observed a tumor in the sella turcica of this kind which gave rise to a Fröhlich's syndrome. Such tumors are demonstrable by the *x*-ray. They are very slow growing.

Fibromata are connective-tissue tumors usually developing from the meninges or from the sheaths of the cranial nerves. They are dense, encapsulated tumors, sometimes multiple, and usually occur at the base of the brain. Their favorite location is in the cerebellopontile angle where they develop from the sheath of the acoustic nerve. They also develop in the vicinity of the Gasserian ganglion. Mixed forms,

such as osteofibroma, fibrosarcoma, fibromyxosarcoma, etc., occasionally occur.

Neurofibromata occasionally occur in the same locations as those given for fibromata. They are frequently multiple, especially when they occur, as in Von Recklinghausen's disease (multiple neurofibromatosis), along the course of the cranial nerves. The nerve fibers contained in them are usually nonmedullated.

Lipomata are comparatively rare in the brain. They are yellow tumors usually well encapsulated and almost always superficial. Their consistency varies according to the amount of fibrous connective tissue they contain. They are almost always basal and may be mixed with other tissue, forming myxomatous lipomata, or sometimes undergo calcification.

Cholesteatomata are usually found accidentally, at postmortem, but they can give rise to the symptoms of brain tumor. Their favorite location, according to Oppenheim, is at the base of the brain in the region of the tuber cinereum or mammillary bodies. Cholesteatomata probably develop from either epithelial nodes (Ziegler) or endothelial formations (Birch-Hirschfeld).

Osteomata are rare tumors in the cranial cavity. Osteofibroma and osteosarcoma are more frequent but not common. They are usually in direct relation to the skull but cases have been reported where they were in the substance of the brain. D. J. McCarthy reports the experimental production of an osteoma in the brain of a kitten by piercing the brain with a wire. Small plates of bone are not infrequently found scattered through the pia-arachnoid. They seem never to produce any symptoms. I have observed them several times in connection with degenerative diseases.

Angiomata occur in the brain in various types—hemangioma cavernosum, telangiectasis, etc.; they are all uncommon. Attention has been called to the frequency with which vascular nevi in the distribution of the trifacial nerve on the face are accompanied by similar conditions in the pia. They are usually congenital and may be the cause of epilepsy or imbecility.

Carcinomata, as primary tumors in the brain, are very rare. They occasionally develop from the choroid plexus or from the hypophysis. Metastatic carcinoma is not uncommon. Starr found forty-three cases of carcinoma out of six hundred cases of brain tumor. The metastasis is through the blood and the tumors are usually multiple. They may be of large size and be encapsulated but are frequently small. In some cases carcinoma cells may be seen in the perivascular spaces all through the brain. A carcinomatous infiltration of the meninges is not uncommon. The histological character of the carcinoma may indicate its origin. Mammary carcinomata most frequently send metastases to the brain but the primary tumor may be in the lungs, esophagus, stomach, adrenal, testes, or other parts.

Teratomata and dermoid tumors are rarely present in the cranial cavity. When they occur they are usually located at the base near the median line.

Cysts are not infrequently present in the brain. They are often the result of degeneration of tumors, especially gliomata, and in such cases have a lining of active tumor tissue. Cysts may also occupy the site of a former hemorrhage or areas of softening. The so-called circumscribed serous meningitis may exert considerable pressure on the brain and give rise to all the signs of brain tumor. Cysticercus and echinococcus cysts are occasionally found in the brain.

The *infectious granulomata* deserve careful consideration, as tumors of the brain, on account of their frequency; tuberculoma being especially frequent in children although present also in adults. The large solitary tubercle is usually located either in the pons or cerebellum; tuberculoma of the meninges, circumscribed tuberculous meningitis, or tuberculosis *en plaque*, usually on the convexity of the brain. They have the histological characteristics of tubercle elsewhere in the body, and the larger ones show caseation.

Macroscopic *gummata* as distinct tumors are not common in the brain although statistics of different authors show considerable variation on this point, depending probably on whether or not gummatous infiltration of the meninges is included as a tumor. Starr includes it and, in a collection from the literature of 600 cases of brain tumor, found gummata twenty-two times. Spiller, in seventy-two cases, found four gummata. Bruns, in thirty-seven cases of brain tumor with necropsy, found no gummata. They occur from acquired syphilis, sometimes within a year after infection (Starr). They are usually located in the cerebral cortex, rarely in the cerebellum, and very rarely in the basal ganglia.

Aneurysms of the cerebral arteries, if of large size, give the symptoms of cerebral tumor. They may be as large as a hen's egg. Authorities are generally agreed that the artery of the fissure of Sylvius is the one most frequently affected and the arteries at the base of the brain are next in frequency. They compress the brain tissue and usually terminate by bursting.

Pathology.—The pathological conditions in the brain the result of the tumor vary with its size and location. The increase in pressure causes a flattening of the convolutions of the brain and, not infrequently, a thinning of the dura mater. In young children the skull may enlarge; in adults the bones are sometimes eroded by the pressure of the tumor, or the pressure of the convolutions on the skull may cause a deepening of the digitiform impressions normally present. Changes may also occur in the base of the skull, widening of the sella turcica, etc., which may be seen by *x*-ray examination. Marked distortion of the brain may be produced by tumors in certain locations, especially those in the cerebellopontile angle. The pressure of the tumor may lead to a marked atrophy of the part of the brain pressed upon without any actual invasion of the tumor tissue. Frequently tumors are surrounded by an area of cellular infiltration or of softening, and occasionally the invasion of a blood-vessel wall by the tumor may cause a cerebral hemorrhage. The circulation of the spinal fluid is frequently impeded giving rise to an internal hydrocephalus. This is of considerable clinical importance as it may lead to pressure symptoms on parts distant from the tumor; for instance, the enlargement of the infundibulum may cause pressure on the pituitary body and on the optic commissure leading to an erroneous diagnosis of tumor of the hypophysis.

Histological examination may show changes in the cerebral cortex such as cell degeneration, increased neuroglia, etc., diffused throughout the brain. Brain tumor, by increasing the intraspinal pressure, causes degeneration of the posterior nerve roots, and posterior columns of spinal cord. The cerebrospinal fluid frequently contains an increased amount of albumin and sometimes shows a xanthochromatic change.

Etiology.—The cause of the development of a cerebral neoplasm is in most cases unknown. Developmental anomalies no doubt account for some of them, especially the teratomata and perhaps also for the angiomata and myxomata.

Many observations have been made on the relation of trauma to brain tumor. There are well authenticated instances in which an area of encephalitis or a splinter of bone has become a starting-point for the development of a tumor. The case reported by McCarthy of the experimental production of an osteoma in the brain of a kitten by inserting a piece of wire shows one way in which trauma could be effective in this connection. Trauma may also act

by exciting to renewed growth a latent tumor. Cases in which the tumor symptoms, headache, etc., began immediately after the trauma are probably of this kind. Traumatic cysts are more common than tumors. Redlich says that it is certain that a traumatism is the cause of many cases of intracranial aneurysm.

Metastasis from other parts of the body accounts for most of the carcinomata and adenomata; and the parasitic cysts usually have a primary focus elsewhere in the body. Solitary tubercle may occur in the brain without any evidence of tuberculosis of the lungs, or other parts of the body open to clinical observation. Gummata of the brain frequently develop in the secondary stage of syphilis and within a year after the infection but may occur in the later stages as well.

Symptomatology.—In some cases a tumor within the cranial cavity may grow to a large size and cause no symptoms indicative of its presence, being found at necropsy when death is due to some intercurrent affection. Such cases are rare. The intensity of tumor symptoms, as well as their character, depends on their rate of growth, their location, and the kind of tumor.

The symptoms may be divided, for the sake of convenience, into the general symptoms, *i.e.* those common to brain tumors in general wherever located; and the localizing symptoms which depend upon the effect of the location of the tumor in interfering with the function of certain parts of the brain. Other factors being equal, the general symptoms are usually more marked when the tumor is located in the cerebellum or in the posterior fossa; whereas, tumors located in the motor area or in the pons will produce focal symptoms first.

Symptoms are also produced by pathological changes in the neighborhood of the tumor, areas of softening, hemorrhages, etc., and by the pressure exerted on parts distant from the tumor through the medium of a dilated ventricle (dilatation of the infundibulum producing pressure on the optic chiasm and hypophysis, for instance).

Disturbances may occur in parts functionally related to the part of the brain affected; a phenomena described by von Monakow under the name of "diaschisis."

The *general symptoms* of brain tumor depend probably upon the increased pressure within the cranial cavity. It is possible, however, that other factors play a part since it is observed that small tumors are sometimes attended with more marked symptoms than the larger ones. The rate of increase in pressure plays an important part. According to Naunyn and Schreiber (quoted by Redlich) the general symptoms are due to a cerebral anemia, the result of the pressure, and for this reason a rapid lowering of the blood pressure in the carotid artery may suddenly make the symptoms manifest. The general symptoms have also been explained as due to a tumor toxin but the uniform nature of these symptoms arising from the tumors of widely different kinds rather militates against this view.

Headache is one of the most frequent symptoms of brain tumor but its occurrence in so many other conditions lessens its diagnostic value. Usually it is also an early symptom, although small tumors in the motor region may cause other symptoms to develop before the headache. Its character is variable, sometimes dull and boring, sometimes neuralgic, sometimes pulsating, especially in aneurysm. Frequently in the early stages it is intermittent, coming on in attacks similar to migraine. This, according to Frankl-Hochwart, is especially true of hypophysis tumors. It may be present only in the morning on arising or may only be brought on by exertion or sudden movement. The location of the pain has no fixed relation to the location of the tumor; frontal headache may be a symptom of cerebellar tumor or the tumor may be on one side of the cerebrum and the pain on the other.

The cause of the pain is probably the stretching of the nerves in the dura by the increased pressure. Not infrequently the pain is a less prominent symptom in the later stages of brain tumor than in the earlier. The numbing of consciousness decreases the perception of the discomfort in some cases; and in others, the erosion of bone or the adjustment of the brain to the altered conditions accounts for the relief. The pain is usually relieved by a decompression operation. Tenderness of the skull on percussion may be a symptom of localizing value. The presence of a bruit usually means an aneurysm; however, it is said to occur over some highly vascular tumors such as angiosarcoma, also in internal hydrocephalus, and a similar sound may also be heard over the skulls of normal young children (Redlich).

A true *choked disc*, especially over two diopters, is a very valuable diagnostic sign of increased intracranial pressure and is rarely absent in brain tumor. According to Redlich, Gowers found it in four-fifths of all cases; Oppenheim in eighty-two per cent.; and Bruns, fifty-one times in sixty-three cases. An optic neuritis is less common. Spiller has called attention to the late appearance of choked disc from glioma of the brain but its very rapid development then. Choked disc is said to develop earliest from tumors in the posterior fossa but I have seen a case of solitary tubercle of the cerebellum in which none occurred. It occurs relatively late in cases involving the motor region or frontal lobes and is rarely seen in tumors of the hypophysis or those in the vicinity of the optic chiasm. The latter usually causes an optic atrophy. Vision is usually little affected by the edema of the nerve head but the prolongation of the condition leads to secondary optic atrophy and a gradually developing blindness.

The pathogenesis of the choked disc is usually ascribed to the increased intracranial pressure. A tumor toxin as the cause seems most unlikely. Usually the edema of the disc develops in one eye earlier than in the other and is more marked in one than in the other. There has been considerable discussion as to whether or not the eye showing the greatest elevation of the papilla indicates the side of the tumor. By most observers it is held that there is no such relation and Walter Parker has shown that the eye in which the edema is more marked is the one which has the lower intraocular tension, and concludes that the development of the choked disc depends on a disproportion between the intracranial pressure and the intraocular tension, thus allowing the disc to be pushed into the eye.

The increased pressure may also account for *deafness* by its effect on the acoustic nerve and Muskens has described *olfactory phenomena* and anosmia as due to the same cause.

Not infrequently the increased intracranial pressure causes a *loss of the knee-jerks* in brain tumor. At necropsy in such cases there is found a degeneration in the posterior columns which begins at the point where the posterior roots enter the spinal cord. It may be attributed to the pull on the nerve roots through their attachments to the cord and spinal dura where there is a distention of the dural sac by the cerebrospinal fluid. A lumbar puncture may cause a return of the reflex (Redlich) under such conditions and I have observed the same thing after a decompression operation.

Mental changes are not uncommon as a symptom of tumor of the brain. In general they are on the order of stupor or dementia. The special mental symptoms depend to some extent on the location of the tumor.

Tumors of the frontal region may produce a mental state somewhat resembling paresis, with an especial tendency to senseless joking, punning, etc., the

"temporosphenoidal" of the German writers. Tumors involving the left temporosphenoidal region and causing word deafness, jargon aphasia, etc., often lead to a mistaken diagnosis of insanity. Mental symptoms are very frequently caused by tumors in the vicinity of the corpus callosum.

Epileptic attacks are frequently caused by tumor of the brain, being present, according to Knapp, in about one-fourth of all cases. Tumors located in or near motor areas may cause Jacksonian attacks which later become generalized. In other cases the general convulsions are present from the beginning and have all the characteristics of epileptic attacks due to other causes. Walton describes a case of cerebral endothelioma in which the chief and practically the only symptom was attacks of epilepsy, both grand mal and petit mal. An operation and removal of the tumor stopped the attacks. Petit mal attacks, or the status epilepticus, may be caused by brain tumor. Attacks of intense sleepiness (narcolepsy) may also be so caused.

Tumors of the cerebellum are often accompanied by peculiar attacks described by Dana as cerebellar seizures, "sudden seizures of violent vertigo, or loss of consciousness, with tonic irregular movements of the limbs, or perhaps only sudden forced movements, throwing the patient to the floor." Oppenheim has also described attacks of tremor or forced movements without unconsciousness and resembling hysterical attacks, as symptomatic of cerebellar tumor.

Vertigo is a prominent symptom in tumors of the cerebellum and its connections, though also caused by tumors in other locations. It may be made worse by sudden change of position and usually bears a fairly constant relation to the headache.

Vomiting is a very pronounced symptom in brain tumor. It is more frequent, as a rule, in tumors located in the posterior fossa. It usually has no relation to the taking of food and is frequently unaccompanied by nausea. The so-called projectile vomiting is regarded as very characteristic of increased intracranial pressure.

Changes in *pulse* and *respiration* are usually late symptoms in brain tumor. Irritation of the vagus nucleus may cause a bradycardia. According to Redlich, this occurs as an early symptom in tumors of the medulla where it is liable to come on in attacks accompanied by vertigo and vomiting. In the later stages a tumor so located would cause an increased pulse rate through vagus paralysis. Respiratory symptoms are also uncommon. In some cerebellar tumors there may be attacks of apnea. Cheyne-Stokes or Biot types of breathing may occur in the last stages of brain tumor.

Other *general symptoms* are not common. The course of a brain tumor is non-febrile. Incontinence of urine may be present in the later stages. Cachectic symptoms are less marked with brain tumors than they are with tumors situated elsewhere in the body. Marked changes in growth and metabolism may occur in connection with tumors in the region of the hypophysis or of the pineal gland.

Localizing symptoms are those by which it is possible to determine in what part of the cranial cavity the tumor is located. Some of the general symptoms may have a localizing value under certain conditions.

Frontal Lobe.—The frontal lobe really includes all that part of the cerebral hemisphere anterior to the cerebral fissure but, by usage, the term is frequently applied to include only the parts anterior to the ascending frontal convolution, the prefrontal lobe. Tumors of the prefrontal lobe are usually credited with the production of certain symptoms such as apathy, intellectual defects, childishness, etc. There is frequently a special tendency to silly jokes, puns, answering questions with others, etc., named, by the Germans, "witzelsucht"; by the French, "puerilité mentale." Tumors at the base of the frontal lobe may cause anosmia through pressure of the olfactory bulb. It is usually unilateral, and local conditions in the nose may interfere with the clinical value of the symptom. Pressure on the optic nerve may cause an optic atrophy which is primary, and not secondary to choked disc such as is usual in brain tumor. Sometimes there is a dilated pupil on the side of the tumor and occasionally exophthalmos. The involvement of the posterior part of the third frontal convolution on the left side usually leads to a motor aphasia, if the patient is right-handed, and to an agraphia if the tumor invades the posterior part of the second frontal convolution. Not infrequently the aphasia is manifested suddenly. It may be, at first, intermittent or consist simply in a slowing of motor speech.

A center for conjugate movement of the eyeballs is also hypothetically located in this region, based upon the observation that epileptic attacks arising from such tumors frequently begin by conjugate deviation of the eyes.

Tumors of the frontal lobe frequently cause an ataxia, cerebellar in type, which may lead to errors in diagnosis. The cause of the ataxia is uncertain but the anatomical connections between the frontal lobe and cerebellum are very intimate and an atrophy of one frontal lobe usually determines an atrophy in the opposite cerebellar hemisphere so that the functional connection is to be expected.

Those tumors of the frontal lobe whose increasing size causes them to involve the precentral convolution give rise to symptoms characteristic of that region, the motor region of the brain.

Motor Area.—Tumors in or near the motor cortex produce definite localizing symptoms and a tumor producing no evidence of its presence in this region would be most unlikely. The motor area is probably entirely comprised in the paracentral convolution and precentral convolution. While there are some who believe that the postcentral convolution is also motor, the former view, based upon the researches of Sherrington, Brodman, and others is the one generally accepted. The earliest symptom of a tumor involving the cortex in this region is usually Jacksonian epilepsy. The attacks are localized in a certain part of the body and consciousness is only slightly, if at all, affected. The part in which the attacks begin indicates the location of the tumor, *i.e.* as in the arm center, leg center, etc. Not infrequently, especially in the later stages, there is some weakness after the attack in the part affected. A continuous twitching may take the place of the ordinary attacks.

As the tumor enlarges and the pressure becomes greater a monoplegia develops which in time progresses to a hemiplegia. The gradual onset of a hemiplegia in this fashion is so characteristic, according to Williamson, that a diagnosis of brain tumor in the motor area might be based on it alone and without the general symptoms of headache and choked disc. The paralysis which develops is of the spastic type, accompanied by contractures, rarely with atrophy, although there is not infrequently some vasomotor change, cyanosis, edema, etc. The reflexes are increased and there is a Babinski reflex on the paralyzed side. Bychowski states that in extracerebral tumors the Babinski reflex is not present, but Redlich claims that this is not a constant sign. There may be no sensory symptoms.

Tumors in the *postcentral convolution* also produce Jacksonian epileptic attacks which, however, usually have a sensory aura, consisting of various parasthesias, in the affected part. The growth of these tumors may lead to the development of a hemianesthesia. As I have shown, the nature and distribution of the sensory changes following lesions to the cortex have certain peculiarities; localization of sensation, discrimination of compass points, and appreciation of light touches are early lost; the distribution of the

lost sensation may correspond to the sensory distribution of the spinal segments.

Tumors located in the *parietal region*, especially the superior parietal convolution, frequently cause a loss of stereognostic perception. The loss of the ability to recognize the shape of objects placed in the hand with the eyes closed may also be due to paralysis or to marked changes in general sense perception.

Tumors in the motor and sensorimotor region, while producing localizing symptoms very early, may not give rise to any of the general symptoms of brain tumor. Redlich refers to such a case, in which there was a glioma of the paracentral lobule; and Walton to a similar case in which an endothelioma was removed by operation. The only symptoms in these cases were Jacksonian epileptic attacks.

Parietal lobe tumors, in general, give rise to sensory symptoms. Those in the ascending parietal usually also cause some motor disturbance secondarily or by pressure. The disturbance of stereognostic sense is the most characteristic phenomenon caused by tumors of the superior parietal region.

Those located in the lower parietal region, in or near the angular gyrus, if on the left side in a right-handed person, cause word blindness, *i.e.* central vision may be apparently normal but the patient is no longer able to comprehend written language. Tumors in this neighborhood may also cause mind blindness, soul blindness, or object blindness as it is variously called. Tumors in the left hemisphere may also cause the amnesic color blindness, described by Wilbrand and Sanger. Spiller has reported such a case and I have also observed an instance of it. If a tumor of this region extends far beneath the cortex, it will interfere with the optic radiations and cause a hemianopsia. Difficulties in lateral associated movements of the eyeballs are sometimes met with in such cases.

Tumors of the *occipital lobe* have for their most characteristic localizing sign disturbances in vision. A hemianopsia or quadrantanopsia is a common symptom. The macular region usually escapes. This symptom may be covered up by the blindness caused by the secondary optic atrophy. Irritation of the cuneus may give rise to various hallucinations usually, however, of a simple character such as sparks of light, stars, etc., but Spiller has described a case of subcortical tumor of the occipital lobe, in which there was no hemianopsia, but in which the patient saw "black objects like snakes, rosettes, and forms of leaves," "and sometimes sees the heads of persons." Tumors on the convexity of the occipital lobe on the left side may cause alexia and such secondary phenomena as agraphia, etc. Pressure on the cerebellum may give rise to ataxia.

The *first temporal convolution* is apparently the cortical center for hearing. Tumors located here, however, do not cause deafness unless they are bilateral. If located on the right side in a right-handed individual they may cause no symptoms. On the left side, they not infrequently cause word deafness, loss of understanding of spoken speech, with, in many cases, a jargon speech and alexia as secondary phenomena. Irritation of this region may cause hallucinations of hearing. These phenomena may occur suddenly and be transitory. There is an interesting observation of Oppenheim, quoted by Redlich, of a case of tubercle of the left gyrus supramarginalis where only on sitting up the pressure of the tumor fell on the first temporal convolution and caused a sensory aphasia.

Lesions in the *second temporal convolution* are also recorded as the cause of agrammatica and amusia. Large tumors in the temporal lobes may extend inward until they press upon the internal capsule and cause a hemiplegia.

Tumors in the *third temporal convolution* may give rise to gustatory phenomena, voracious appetite, etc., and may, by extension, involve the optic tract causing hemianopsia and may also cause pressure on the hypophysis.

Tumors of the *gyrus hippocampus* may give rise to a peculiar dreamy state (Jackson).

Tumors of the *uncinate gyrus* frequently give rise to epileptic attacks ushered in by an aura of the sense of taste or smell; the so-called "uncinate group of fits" (Mills).

Tumors of the *corpus callosum* are characterized chiefly by the late appearance of the general symptoms of brain tumor and paralysis, although there are exceptions. The most prominent symptoms are usually mental. Putnam and Williams found, in thirty-eight cases, only four without mental symptoms. The symptoms are usually of the character of apathy or dementia. Recent studies by Liepmann and others have shown that apraxia is a characteristic of lesions in this vicinity. A hemiparesis not infrequently develops, also a peculiar form of ataxia has been described which closely resembles the ataxia due to frontal lobe tumors.

Tumors in the *white substance of the frontal, parietal,* or *temporal* lobes can exist for a long time without producing any localizing symptoms, but sooner or later the projection fibers from the motor cortex or to the sensory or special sense areas are involved and paralysis or anesthesia results. In such cases the distribution of the paralysis is likely to be more widespread than in the case of a cortical tumor—a hemiplegia rather than a monoplegia. Jacksonian epileptic attacks may occur, but are neither so early nor so sharply localized as in cortical tumors.

Tumors in the region of the *lenticular nucleus* cause hemiplegia from pressure on the internal capsule; if the posterior limb of the capsule is involved there may also be hemianesthesia and hemianopsia. Tumors in this region may also cause dysarthria and if on the left side of the brain, an aphasia. Czyhlarz and Marburg have described disturbances in micturition produced by tumor in this location.

Tumors of the *optic thalamus* usually produce hemianesthesia and hemianopsia; a hemiplegia may be caused by pressure on the internal capsule and also Jacksonian epileptic attacks. Cases have been described in which there was a continuous tremor in the opposite half of the body, but this symptom was probably due to irritation of the red nucleus. The so-called "central pain," *i.e.* pain referred to the extremities and due to irritation of the sensory fibers in the brain, is a symptom of lesions of the thalamus. Tumors in this region may cause a unilateral exophthalmos and pupillary irregularity.

I have observed a case with necropsy in which a tumor in the thalamic region caused a blocking of the foramen Monro and a hydrocephalus affecting only the posterior horn of the lateral ventricle.

Tumors in the *midbrain* cause pronounced localizing symptoms very early in their development and a very small difference in their location produces a marked difference in the nature of the symptoms.

Tumors of the *anterior portion of the cerebral peduncle*, the foot of the peduncle, produce the so-called syndrome of Weber, *i.e.* oculomotor paralysis on the same side as the tumor and a spastic paralysis of the extremities on the opposite side. Tumors in the posterior portion produce the syndrome of Benedict, oculomotor paralysis on the side of the tumor and choreic movements or tremor in the extremities on the opposite side. Tumors of the corpora quadrigemina are usually characterized by oculomotor palsy, ataxia and some disturbance in vision or hearing, depending on whether it is the anterior or posterior pair that is involved. The oculomotor paralysis usually appears in some muscles earlier than others, indicating the probability of a nuclear origin.

Tumors of the *pineal gland* are not common. They

are usually psammomas or teratoid growths and cause symptoms similar to those caused by tumors of the corpora quadrigemina but, in addition, may be accompanied by evidence of disturbances in the internal secretion of the gland, shown by disturbances in growth, nutrition, and secondary sexual characteristics.

Cerebellar tumors may at times cause very few symptoms, especially the solitary tubercle (common in children) and the glioma. In the majority of cases, however, there are very distinct localizing signs. The most important signs of cerebellar involvement are the special disturbances in coordinate movements. This is frequently first noticed in walking, as a staggering gait, like that of a drunken man. It is usually not much affected by closing the eyes. In tumors of the vermis the tendency is to fall either forward or backward, especially the latter, or to either side. In tumors of a cerebellar hemisphere the tendency is generally to fall toward the affected side. An ataxia on motion may be noticed in all four extremities, or only on the side of the tumor. The ataxia on motion may be accompanied by an increased ability to hold the extremity steadily in one position, "cerebellar catalepsy." Babinski has called attention to a symptom which he calls adiadochocinesia, consisting of a disability or inability to reverse rapidly a simple movement, pronation and supination of the hand, flexion and extension of the elbow, and so on; also to a lack of the normal synergy of the muscles of the body and extremities—the cerebellar asy nergy shown in throwing movements, etc.

Vertigo is usually a pronounced symptom in cerebellar tumor. It may come on in attacks similar to Ménière's disease. Dana has described, under the name of cerebellar seizures, attacks in which the vertigo is accompanied by a loss of consciousness and forced movements. According to Stewart and Holmes, the subjective sensation produced by an intracerebellar tumor is that the surroundings are whirling around the patient from the side of the lesion to the sound side; in extracerebellar tumors this is reversed, the surroundings appear to be moving from the sound side toward the side of the lesion.

The head is likely held inclined toward the side of the tumor and, according to Schmidt, lying with the opposite side of the head downward increases the symptoms because the weight of the tumor presses on the cerebellum. There may be some pain and rigidity of the back of the neck.

A light hemiparesis with an atonic condition may develop on the same side as the tumor. This is in marked contrast to the hemiplegia developing from cerebral tumors which is always hypertonic. I have observed a loss of the umbilical and cremasteric reflexes on the same side as the tumor in one of these cases.

Nystagmus is an important symptom of cerebellar tumor. It is a spontaneous nystagmus, either horizontal or vertical, and the labyrinth reacts normally to the caloric and turning tests.

The general symptoms of brain tumor are frequently very severe in cerebellar tumors, especially the headache and choked disc. Mental symptoms are usually less marked. Epileptic attacks may occur, but they are usually of a peculiar character with opisthotonus, etc., and may resemble hysterical attacks. Vomiting and changes in the pulse and respiration may be marked symptoms. Pressure on the fifth nerve may cause neuralgic pain in its distribution and frequently causes a loss of the corneal reflex on the side of the tumor. The facial nerve may also be pressed upon causing a facial palsy. These tumors may be accompanied by a loss of the deep reflexes in the extremities, owing to the degeneration in the posterior spinal nerve roots.

Tumors in the *cerebellopontile angle* are not uncommon. They are fibromata or fibrosarcomata as a rule, and grow usually from the sheath of the acoustic nerve. The first symptom is almost always a unilateral nerve deafness accompanied by a facial palsy of the peripheral type on the same side. The further growth of the tumor causes pressure on the pons and cerebellum and some symptoms from both these locations. There is usually an external rectus paralysis on the same side as the tumor and sometimes on both. The gait is that of a cerebellar ataxia.

Tumors may also grow from the sheath of the *fifth cranial nerve* or the *Gasserian ganglion* giving rise to trifacial neuralgia as an early symptom and later to a paralysis of the muscles of mastication and anesthesia of the face on the same side.

Pons.—The most characteristic symptom of tumor of the pons is the so-called Gubler syndrome, paralysis of the cranial nerves especially the fifth, sixth, and seventh on one side and of the opposite half of the body. Though, in general, localizing symptoms develop early in these cases; the solitary tubercle, not infrequent in this location especially in children, may be latent for a long time. In the early stages of these tumors irritation of the fifth nerve nucleus may cause neuralgic pains in the face and trismus, or irritation of the seventh nerve cause a facial spasm. Spiller has called attention to the resemblance of some tumors of the pons to tumors of the Gasserian ganglion in causing trifacial neuralgia. The later destruction of these nerve nuclei leads to a paralysis which has the character of a peripheral nerve palsy. Dissociation of sensation in the face may result from pontile tumor. There is usually some weakness in the external rectus but that is such a frequent finding in brain tumor in any location that its localizing value is lessened.

The important symptom of intrapontile tumor is the paralysis of lateral associated movements of the eyeballs. If a unilateral tumor, this paralysis is on movement toward the side of the tumor. Spiller regards it as a very valuable sign to differentiate between intrapontile tumors and tumors outside the pons but pressing on it and causing similar symptoms. If the tumor is in the dorsal part of the pons the involvement of the pyramidal tracts may not come on until late in the case. Involvement of these fibers may cause Jacksonian epileptic attacks by irritation, or their destruction may lead to a spastic paralysis of the opposite half of the body.

Tumors of the *medulla* cause symptoms similar to those of the pons, *i.e.* a crossed paralysis, the lower cranial nerves on one side, the side of the tumor, and a spastic paralysis of the opposite half of the body. Such symptoms may be caused by slowly developing cavities in the bulb, syringobulbia. The descending root of the fifth nerve when affected leads to an anesthesia in the distribution. Tumors high in the medulla may cause deafness and facial palsy; situated lower they cause paralysis of the hypoglossus, with atrophy, dysarthria, dysphagia, etc., the symptoms of bulbar palsy. The involvement of the pyramidal tracts may be unilateral or bilateral; in the latter case there would be a spastic paralysis of all four extremities. It should be remembered that bulbar symptoms may be caused by a toxemia and may occur with carcinoma of parts other than the nervous system, as in a case reported by Weisenburg.

The *fourth ventricle* is a favorite site for brain tumors. They are usually gliomata and grow from the floor of the fourth ventricle completely filling it and invading the cerebellum through its roof. The symptoms of an intrapontile tumor may be present, including the paralysis of lateral associated movements of the eyeballs. The growth of the tumor into the cerebellum may cause a cerebellar ataxia but, since the tumor is in the median line, the special symptoms indicating the side affected will be absent.

The occlusion of the fourth ventricle causes an internal hydrocephalus which may lead to the dis-

charge of cerebrospinal fluid from the nose or cause a bitemporal hemianopsia from the pressure of the dilated infundibulum on the optic chiasm. Polyuria, glycosuria, and changes in pulse and respiration are reported as occurring in such cases.

Tumors growing from the dura or base of the skull and pressing upon the brain cause varying symptoms, according to the part pressed upon. Tumors of the hypophysis are treated of in another place.

Multiple tumors and tumors infiltrating the meninges frequently cause no localizing symptoms or the symptoms of but one tumor may be present when multiple tumors are disclosed by necropsy. In cases of von Recklinghausen's disease the tumors are frequently multiple. Metastatic carcinoma and sarcoma, melanosarcoma, etc., are frequently either multiple or infiltrate the meninges; and endotheliomata sometimes grow as multiple tumors from the dura. Tumors infiltrating the meninges may sometimes be diagnosed by lumbar puncture either by the golden yellow color of the fluid (Rindfleisch, Kleineberger) or by the presence of tumor cells in the fluid (Kronig, Rindfleisch, Widal, Sicard and Gy, and others).

Course.—The course of a brain tumor is usually slowly progressive. It depends on the location whether the general or localizing symptoms appear first. The first complaint may be either of headache, of visual disturbance, or of epileptic attacks, and I have had a patient who was treated for vomiting spells, supposedly due to some stomach trouble, for over a year before other symptoms arose indicating a brain tumor. Sometimes the early symptoms are purely psychic and the patient is regarded as insane. Many cases of brain tumor are in asylums, undiagnosed. In some cases the symptoms begin suddenly, apoplectic strokes, aphasia, etc., due probably to a hemorrhage into the growth.

There are frequently marked variations in the symptoms, periods of improvement or even an intermission in symptoms. This is especially the case in tubercle and gumma but is also found in highly vascular tumors, due to variations in their blood content, and in tumors causing hydrocephalus. A tumor may erode its way through the skull or into the sphenoidal sinus or pharynx thus relieving the pressure on the brain.

The duration of life with brain tumor is very uncertain as it depends on the nature and rapidity of growth of the tumor and on its location, especially the latter. Tumors in the cerebral hemisphere may attain a large size without causing death.

The actual cause of death from brain tumor may be an apoplectic attack; status epilepticus; sudden interference with respiration, especially in tumors at the base; or some intercurrent disease such as pneumonia, cystitis, nephritis, etc. Spontaneous recovery is very rare. Tubercles may stop growing and become calcified. Cysts due to echinococcus or cysticercus may stop growing, so also may some tumors such as osteoma, psammoma, or cholesteatoma, and possibly others. Redlich is of the opinion that most of the cases of brain tumor with reported spontaneous recovery were cases of so-called pseudotumor.

Diagnosis.—The diagnosis of the presence of tumor of the brain will depend upon the presence of the general symptoms of increased intracranial pressure and in addition some signs indicating a localized lesion. At times the diagnosis is made upon the general symptoms alone or upon the localizing symptoms alone, but either course is hazardous.

The general symptoms are primarily due to the increase of intracranial pressure and this may be due to many other causes than brain tumor. Headache is such a frequent complaint and due to so many pathological conditions that its diagnostic value is small, as a sign of brain tumor. Headache resembling that caused by brain tumor is seen in migraine, in various anemias, in neurasthenic and hysterical individuals, in arteriosclerosis, in uremia, autointoxication, chronic meningitis, and syphilitic periostitis. The psychic symptoms due to brain tumor have no special characteristics which by themselves would lead to a correct diagnosis. The general epileptic attacks cannot be differentiated from epilepsy due to other causes and the Jacksonian attacks may be due to other irritative lesions of the cortex such as a cortical hemorrhagic encephalitis, as in a case reported by Mills. The occurrence of epileptic attacks late in life should always lead to a suspicion of brain tumor. Vertigo is a symptom which is also common in many affections, such as disease of the labyrinth, arteriosclerosis, circulatory disturbances from heart lesions, intoxications, etc. Choked disc, while a symptom highly suggestive of brain tumor, may also be present in other conditions, notably hydrocephalus, brain abscess, sinus thrombosis, pachymeningitis, etc.

The individual symptoms are of less value than a combination of several of them but all of them may be present in cases of internal hydrocephalus, serous meningitis, and the so-called pseudotumor cerebri, sinus thrombosis, brain abscess, acute encephalitis, multiple sclerosis, and paralytic dementia. The acute hydrocephalus is frequently caused by a brain tumor which blocks the flow of cerebrospinal fluid from the ventricle. Such cases may sometimes be recognized by the relatively sudden increase in symptoms, the development of a bitemporal hemianopsia through the pressure of the infundibulum on the optic chiasm; through puncture of the ventricles; or, as Spiller has pointed out, by an *x*-ray examination of the skull which in these cases of acquired hydrocephalus show digitiform markings corresponding to cerebral convolutions. Meningitis serosa or pseudotumor often cannot be clinically differentiated from brain tumor. The history of the case may aid—a history of trauma, sunstroke, or aural infection followed by the rapid development of the symptoms for instance, but the history is often negative. The absence of definite localizing symptoms is probably the most reliable means of differentiation though it should be remembered that serous meningitis may cause signs of cerebellar disturbance such as nystagmus, etc. Autochthonous sinus thrombosis may cause the symptoms of brain tumor without the edema of the scalp, epistaxis, or marasmic origin, which are the signs usually depended upon to make the diagnosis, as in a case reported by Riggs.

The diagnosis of brain abscess usually depends upon a possible etiology and the presence of some symptoms of infection such as fever, leucocytosis, etc. These, however, may all be absent and as some cases of brain abscess run a very slow course the resemblance to brain tumor is very close.

As between multiple sclerosis and brain tumor, the symptoms in favor of the former are the pallor of the temporal side of the optic discs, the remittent course, bladder symptoms, scanning speech, and the absence of the abdominal and cremasteric reflexes. Dementia paralytica may be mistaken for brain tumor but the Argyll-Robertson pupil and other signs of syphilis and the cytological and chemical findings in the cerebrospinal fluid usually suffice to distinguish, clinically, between them.

The use of the Roentgen ray may be of value in the diagnosis of tumor of the brain in some cases, especially where the tumor is more dense than the surrounding brain substance, as in psammoma or osteoma, or where the tumor is so situated that it changes, by its presence, the conformation of the bone, the widening of the sella turcica by a tumor of the hypophysis for instance. Another diagnostic aid is brain puncture. A small hole is bored through the skull and the brain punctured with a hollow needle. In this way a core

of the substance through which the needle passes may be obtained for histological study.

Localization.—The diagnosis of the localization of brain tumor has made great strides in recent years but it is a subject still beset with difficulties. This is especially true of certain parts of the brain sometimes spoken of as silent areas, the chief of these being the frontal lobe, especially the right; and the right temporosphenoidal lobe. Whereas, as we have seen, a tumor located in most parts of the brain would, by the disturbance caused there, produce a characteristic symptom complex, lesions in these silent areas seem to be without effect on brain function. A special difficulty arises in the diagnosis of tumors of the frontal lobe from those of the opposite cerebellum. Choked disc usually develops early in the latter case. The diagnosis of extrapontile tumors pressing on the pons from intrapontile tumors is perhaps best made by the finding of a paralysis of lateral associated movements of the eyeballs in the latter. The diagnosis of cortical from subcortical tumors is of great importance. As a rule, the cortical irritation is more likely to cause Jacksonian epileptic attacks than the subcortical, but the safer method of differentiating is by a study of the order and rapidity of progression of the symptoms. Spiller has called attention to softening of the dentate nucleus as a cause of symptoms resembling those of cerebellar tumor and has reported such a case. Buzzard has reported a similar case. The *x*-ray may also aid in the localization of a tumor in certain cases.

A *diagnosis of the kind* of brain tumor present is not usually attempted. Certain kinds of tumor, however, are so regularly found in certain locations that an inference can be drawn from the location as to the nature of the growth. Tumors in the cerebellopontile angle are almost always fibroma or fibrosarcoma. Those of the Gasserian ganglion are endothelioma. Cerebellar tumors are usually either glioma or solitary tubercle. Tumors in the ventricles are either glioma or adenoma from the choroid plexus. Endotheliomata are usually on the surface of the cerebrum and, according to Walton, are to be suspected when the general symptoms of brain tumor are slight or absent. The kind of tumor may also be inferred by the density of the shadow cast in a radiograph and may be directly studied by finding tumor cells in the spinal fluid, or by a brain puncture. Syphilitic tumors may be detected by the presence of the Wassermann reaction, especially if it is present in the spinal fluid. Theoretically tubercle should be detectable by the Calmette or von Pirquet reactions but in my experience these reactions have been absent in cases which necropsy showed to be tubercle. Carcinoma elsewhere in the body, especially in the breast, makes it likely that a tumor of the brain in the same patient is a metastasis. Serum reactions for carcinoma, sarcoma, etc., have not reached a point where they can be depended upon for the detection of these conditions within the cranial cavity.

Treatment.—The treatment of tumors of the brain may depend to a great extent upon their location and the nature of the growth. Medicine is not of much avail, outside of the antiluetic treatment for gumma. It has been claimed that the use of potassium iodide in large doses may inhibit the growth of tumors although it cannot usually be proved that these were not cases of pseudo-tumor, hydrocephalus, and so on. Redlich mentions having seen a case of brain tumor in which the administration of mercury caused a marked improvement in the symptoms of Jacksonian epilepsy, paralysis, choked disc, and headache; an operation showed that the tumor was an endothelioma. It has been noted by Noethe and also by Jooss that an intravenous injection of salvarsan is liable to cause a rapidly fatal termination in cases of brain tumor apparently because it causes an extravasation of blood into the tumor. Medical treatment of the symptoms of brain tumor is also unsatisfactory. The headache may often be relieved temporarily by application of cold, absolute quiet, etc., but when severe is not relieved even by large doses of morphine. During the attacks of vomiting no food should be given but small pieces of ice may be kept in the mouth and the patient should be warned against any rapid change of position. The most promising method of treatment of brain tumor is by surgical measures. In a certain percentage of cases the tumor is of such a kind and is so situated that it can be removed surgically, but an accurate diagnosis of the location and a thoroughly efficient operative technique are absolutely necessary for a favorable result. Constant improvement in the art of localization and in surgical appliances is gradually increasing the number of successful brain operations.

If it is decided that for any reason the tumor is irremovable it may be of great benefit to remove a part of the skull in order to reduce the intracranial pressure and relieve such symptoms as the choked disc, intolerable headache, or dangerous vomiting, thus prolonging the life of the patient and adding greatly to his comfort. These so-called decompressive operations may be done over the part of the brain suspected of containing the tumor or else done in the right temporal region. The reasons given for selecting the latter site are: the accessibility; the right temporosphenoidal lobe is a so-called silent area in right-handed people and, therefore, a hernia of this part of the brain causes fewer symptoms; and the temporal muscle is supposed to afford some protection to the brain when the skull is removed. The last reason, however, is of small account, in my experience, as the development of a cerebral hernia is the usual result of these operations and the temporal muscle then atrophies. The intracranial pressure may also be reduced by lumbar puncture or by puncture of the ventricles. The former is a dangerous procedure in brain tumor as a number of deaths have been reported as caused by it. The explanation of these deaths is that the medulla is drawn down, or pushed down into the foramen magnum by the pressure from above when the pressure in the spinal canal is lowered. The pressure of the edges of the foramen magnum on the medulla causes interference with its vital functions and sudden death. Puncture of the ventricle would seem to be less dangerous in such cases but is considerably more difficult and requires more equipment.

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Williamson, R. T.: Practitioner, 1904.

Brainard, Daniel.—Born in Whitesborough, New York, in 1812. He received the degree of Doctor of Medicine from the Jefferson Medical College, Philadelphia, in 1834. He began to give lectures on anatomy and surgery in the Oneida Institute, and in 1836 removed to Chicago. He went to Europe

Fig. 1086.—Daniel Brainard.

in 1839 and returned in 1841, when he was appointed Professor of Anatomy in the University of St. Louis, Missouri. He later moved to Chicago and took an active part in organizing the Rush Medical College, which received its charter in 1837 and opened in 1843. Brainard occupied the Chair of Surgery. He died in 1866. A. H. B.

Branchiogenic Cysts and Fistulas.—No part of the body is so frequently the seat of congenital tumors as the lateral regions of the neck bounded roughly by the floor of the mouth above, anteriorly by the jugulars, below by the clavicle, and posteriorly by a line dropped from the mastoid process, the so-called *branchial regions*. Cystic tumors of these regions are of very frequent occurrence in operative surgery and in practical pathological diagnosis, although in some of the surgical text-books of the day they are said to be rather rare. An analysis of these cystic tumors of the lateral cervical areas shows that they represent a number of widely separated and unrelated pathological conditions, although most surgeons and some pathologists group them all under the head of "branchial cysts." For example, Senn in his article in the second edition of this Handbook divides branchial cysts into four principal varieties: mucous, atheromatous, serous, and hemato-cysts, a classification based wholly upon the cyst-contents, without reference to the origin or structure of the cyst itself. It is obvious that such a basis of classification has no pathological value, inasmuch as the character of the contents does not in many cases throw any light upon the nature or origin of the cyst. From their histological structure these cervical cysts must be classed as: (1) *Epithelial*, lined either by squamous cells (mucous-membrane cysts, ectodermal cysts, dermoids, or epidermoids) or columnar cells (mucous-membrane or entodermal cysts); (2) *angiomatous tumors* with large cavernous spaces; (3) *lymphangiomatous tumors* of the nature of cystic or cavernous lymphangiomata (*cystocele, hydrocele,* or *hygroma colli con-*

genitum). It is evident that only the cysts belonging to the first class, the epithelial cysts, can be regarded as definitely branchial in origin, that is, as arising from remains of the branchial clefts, and they alone should be classed as *branchial cysts*. Since the term *branchial* has, however, been applied to all the cysts and tumors arising in the branchial region, the cysts of true branchial origin may be more properly styled *branchiogenic*, as indicating both their structure and origin. Of the same nature and origin are the congenital lateral cervical fistulas (*branchiogenic fistula, fistula colli congenita*), and they should be treated in the same connection.

Origin.—In the fetus of four weeks' development there are formed on either side, just back of the head, in the region later to be the cervical area, four clefts or grooves and five branchial arches, the last arch lying posteriorly to the fourth cleft, and not being sharply defined along its posterior margin. These clefts are the analogues of those that exist in the walls of the pharynx of fishes through which the water taken in at the mouth passes outward, bathing the gills attached to the gill arches. These analogous clefts and arches in the human embryo are called *branchial*, although they are not normally openings entirely through from the skin to the pharynx, and never possess any respiratory function. Corresponding to each groove in the ectoderm there is one in the entoderm (*branchial pocket*), so that in the region of the groove the ectoderm and entoderm are in close relation, having only a thin wall of mesoderm between them, while in the arches separating the clefts there is a much greater amount of mesoderm. The branchial arches and clefts are of great morphological importance, as they determine largely the development of various parts of the face and head. The first cleft is closed normally by a fold growing backward from the posterior edge of the first arch to unite with the ventral part of the anterior border of the second arch, only the upper part persisting to form the external auditory meatus, while the pinna of the ear is developed from the adjacent parts of the first and second arches. The region of the three posterior arches and clefts becomes depressed to form the *sinus præcervicalis*, the anterior boundary of the sinus being formed by the posterior edge of the second arch, while its posterior boundary is formed by the thoracic wall. Later these two boundaries approach and fuse together converting the sinus into a completely closed cavity the floor of which is formed by the ectodermal covering of the three posterior arches and intervening clefts. Normally this cavity should entirely disappear so that no traces of it are found in the adult body. The entodermal pockets or grooves between the branchial arches internally develop further by the conversion of the first into the tympanic cavity and Eustachian tube; the upper portion of the second internal groove disappears but the lower portion persists as the tonsillar fossa; the lower portions of the other two are represented by the sinus pyriformis of the larynx and by the branchial epithelial bodies that take part in the formation of the thyroid and thymus.

As the result of disturbances in the development and closure of the external and internal clefts various malformations may arise, according to the degree and location of the disturbance. A failure in part of the normal closure or a fusion of the clefts or cervical sinus leads to the formation of persistent *fistulas*, either complete with both external and internal openings, or incomplete with either an external or internal opening; or of closed *cysts*, either ectodermal or entodermal. The remains of the internal grooves may form diverticula of the pharynx, larynx, or trachea, or congenital sacs and pockets in the neighborhood of the tonsils or Eustachian tube. Disturbed development of the posterior ends of the lower three clefts may give rise to the formation of the malformation known as "cervical auricles"; it is also probable that some of the dermoid cysts of the floor of the mouth, thyroid, and thymus arise from remains of the "epithelial bodies" derived from the lower portions of the lower internal branchial grooves and which take part in the formation of thyroid and thymus. Accessory thyroids also take their origin from these bodies.

Structure.—The most common form of the true branchiogenic cyst has an internal lining of squamous cells that do not undergo cornification. The cyst is filled with a soft or semi-fluid, or even fluid, or pultaceous mass consisting chiefly of disintegrated epithelial cells. Beneath the epithelium there is a zone of lymphoid tissue containing germ-centers. The inner wall of the cyst may be smooth or may present projections or crypts, so that there is a striking histological resemblance between sections of the wall of these cysts and sections of the tonsil; so close is this resemblance that individual sections cannot be differentiated. Mucous glands I have never seen in these cysts, but branchiogenic cysts containing both squamous- and columnar-celled areas have been described. In such cases the resemblance to the mucous membrane of portions of the upper respiratory tract may be very close. Areas of cartilage have also been described as occurring in the cyst wall. In a relatively large series of cases of cysts from the branchial areas I have never seen cartilage. The great majority of my cases have been of the type just described, with walls resembling in structure the mucous membrane in the region of the tonsils, and must, therefore, be regarded as *entodermal* in origin, arising from the internal branchial pockets, most probably from the lower portion of the second. Such branchiogenic cysts are usually classed as branchial *dermoids* or *epidermoids*, but it is obvious from their structure that they are not ectodermal, and some pathological distinction should be made. As far as I have been able to discover, Ribbert is the only writer who mentions the histological resemblance of the wall of these cysts to the tonsil, and he does this only incidentally. Cysts of this type are practically snared-off pockets or diverticula of the pharynx, and might be styled *pharyngocysts*, as an indication of their histological structure. They are found most frequently in the upper part of the neck between the hyoid bone and the mastoid process. True *branchiogenic dermoids* and *epidermoids* are much less common. They contain atheromatous, sebaceous, or pultaceous material (*atheromata*), and have a thinner, but firm wall of connective tissue, rather sharply outlining them from the cervical tissues. The cyst is lined with squamous cells showing more or less horny change. Some show hair-follicles and sebaceous glands in the wall (true dermoids), but these are rare. Also rare are the cysts lined by columnar or ciliated epithelium, with serous or mucoid contents (also called *hydrocele* or *hygroma colli congenitum*). Multilocular serous cysts have also been described as branchiogenic, but it is probable that they belonged to the cystic or cavernous *lymphangiomata* (also classed as *hydrocele, cystocele*, or *hygroma colli congenitum*) that are not rare in this region. Such tumors consist of greatly dilated and tortuous lymphatics separated by connective-tissue trabeculæ containing lymph-nodes or germ-centers. It is probable that they arise as the result of a lymph-stasis. The so-called branchial hematocysts are either hemorrhagic epithelial cysts or hemangiomata, that are not branchiogenic.

The contents of the branchiogenic cysts will depend upon the character of the epithelial lining. With squamous epithelium showing a tendency to cornification it will be atheromatous or pultaceous;

with squamous cells of the mucous membrane type the contents will be semi-fluid, or thin and serous, while if the epithelium is columnar it may be mucoid. When both squamous and columnar cells are present the contents may be mixed in character. Blood or pus may be present as the result of secondary changes, or complications (hemorrhage, infection, etc.).

The *external branchiogenic fistulas* are usually found at the side of the neck, more rarely nearer to the median line, and are the result of a failure of the cervical sinus to close completely; the internal fistulas open into the pharynx, trachea, or larynx, in the majority of cases near the tonsil. Often the remains of the internal pockets form only depressions, sacs, or diverticula of these organs. The complete branchiogenic fistula with both external and internal openings is rarely seen. The orifices of the external fistulas are often so small as to be seen with difficulty as minute points; but small round depressions with central conical orifices, or even fissures with valve-like outlets may be found. The openings may be so small as barely to admit the finest probe, or they may be open and free. They are usually near the border of the sternomastoid, sometimes as low as the upper border of the sternum. The fistula is lined with mucous membrane, either squamous, or columnar, or ciliated. It may secrete a mucoid fluid. The course of the fistula may sometimes be traced upward as a cord-like or indurated tract, often running a very tortuous course.

Symptoms.—The branchiogenic *cysts* usually cause no symptoms beyond the disfigurement caused by the tumor. The swelling may be present from birth, or may develop soon after, or its development may be delayed until after puberty or in adult life. It appears usually as a slowly growing, painless, soft cyst, causing no symptoms unless through pressure, or infection, which is not uncommon. They are most common along the anterior border of the sternomastoid. They may increase in size until they occupy the greater portion of the anterolateral cervical region.

The branchiogenic *fistula* may also cause no symptoms, and may not be discovered until infection has occurred. This is particularly likely to be the case with the external fistula, which usually secretes little fluid. In the case of the complete fistula there is a greater amount of secretion, and particles of food may enter from the pharynx, causing irrittaion and inflammation. A complete fistula may also cause trouble in the playing of wind instruments. The lining of the fistulas is very sensitive; probing almost always produces a spasmodic cough as if the mucosa of the larynx had been touched. It is necessary, therefore, to cocainize the canal before sounding.

Diagnosis.—The branchiogenic *cyst* is rarely diagnosed clinically, except as one of the possibilities of this region. The tumor is in the majority of cases diagnosed clinically as tuberculosis of a cervical lymph-node, and the correct diagnosis made only when it is cut into or examined microscopically. Fluctuation is rarely present except in the mucoid cysts (hydrocele). It may also be mistaken for a lipoma. From the cavernous and cystic lymphangiomata the branchiogenic cysts may be differentiated by the larger size, more rapid growth of the former, presence of fluctuation, and their tendency to form a sort of collar around the neck extending backward. Aspiration may be used as an aid in diagnosis. A sudden increase in size of the lymphangioma usually indicates a hemorrhage. Congenital hemangioma hypertrophicum is also not rare in this region. A differential diagnosis is not made usually until the growth is opened. Aneurysm, accessory thyroid, tumor of the carotid gland, metastatic malignant tumors in the cervical lymphatics, syphilis and actinomycosis of the lymphatic glands, etc., must also be considered in the differential diagnosis, which is not easy, and often impossible, before operation. The chief points in the diagnosis are the location, and the slow growth of a soft or cystic tumor, *not preceded by a solid tumor*.

In the case of the branchiogenic *fistulas* the diagnosis is easy when there is an external opening, but often missed in the case of the internal fistula. The external fistulas need only to be differentiated from the *thyroglossal fistula* found in the median line, and having an entirely different origin, and from a purulent fistulous tract. Their fixed location aids in distinguishing them from lymphatic or retention-cyst sinuses. When inflamed and obstructed the picture may be that of cervical abscess or phlegmon, and a differential diagnosis may at times be impossible. Internal fistulas may be located by proper local inspection of the pharynx, larynx, and trachea. The internal openings are usually in the neighborhood of the tonsils.

Prognosis.—The prognosis for a cure without operation is bad. Spontaneous disappearance of the tumor or closure of the fistula is very rare. The prognosis in operations upon the branchiogenic cysts is usually very good in the hands of a skilful surgeon who knows well the anatomy of the region, and the close relation of the tumor to the important structures there. The prognosis in the case of the branchiogenic fistula is not so good, as operation is often difficult or impossible, and other measures fail to relieve.

Treatment.—Operation offers the greatest possibility of cure. In the case of the cysts the excision may not be difficult, but sometimes the most careful dissection is necessary to avoid the injury of neighboring structures of importance. The difficulties are still greater in operating upon the fistulas. From the tonsillar or pharyngeal regions the fistula passes downward over the pharyngeal and hypoglossal nerves, passes under the stylopharyngeus and styloglossus muscles, along the great vessels, between the external and internal carotids, across the digastric muscle to an exit near or between the borders of the sternomastoid, sometimes as low as the upper border of the sternum. The removal of such a tract, particularly if adherent to its surroundings, becomes a very difficult operation which only an experienced surgeon should undertake. Even in the best hands the removal of the fistula may be impossible. The partial removal is of no avail; if even small portions of the epithelial lining are left recurrence or cyst formation is the rule. When complete removal is impossible careful drainage and cleansing of the cavity may be followed by a cessation or lessening of the discharge, and a diminution in the size of the lumen. Other methods of obliterating the cavity by caustics, cautery, injection, scraping, etc., are now condemned by the best surgeons as useless, as it is practically impossible to destroy all of the epithelial lining in this way. Therefore, if the patient does not object to the disfigurement of a large scar, operation should be performed. Injections of methylene-blue into the tract, or the introduction of flexible probes may be utilized as a guide to the operation. If such aids are not used, the course of the sinus may be lost before its end is reached, as it does not differ in color or texture from the surrounding tissues. The operator should endeavor to remove all of the wall of the fistula. Any part left behind will develop a cyst or another fistula.

Branchiogenic Carcinoma.—The most important characteristic of both branchiogenic cysts and fistulas is their tendency in middle life to become carcinomatous. That this must be relatively frequent is shown by the large proportion of such cases

occurring in the pathological service of my laboratory in the University of Michigan. Two types of primary carcinoma in the branchial region occur, both squamous celled; one is *medullary*, without any tendency to the formation of epithelial pearls, and is very malignant. It is in all respects like the squamous-celled carcinoma of the mouth cavity and esophagus, and, therefore, must be regarded as arising from the entodermal cysts. The *horny* or *cancroid* type, with epithelial pearls, is much more rare, and is less rapidly malignant. It runs about the same course as the lymphatic secondaries in the neck from the primary squamous-celled horny cancer of the lip. The differential diagnosis of branchiogenic carcinoma rests upon the exclusion of any primary squamous-celled carcinoma in the regions contributory to the lymph-glands of the branchial regions (mouth, lips, nose, tongue, pharynx, tonsils, larynx, trachea, esophagus, salivary glands, etc.), or, to be absolutely sure, of the existence of any other primary squamous-celled carcinoma in any other part of the body. When such exclusion is determined the development in the lateral regions of the neck of a squamous-celled carcinoma is to be taken as positively branchiogenic in origin. I have seen all stages of development of these branchiogenic carcinoma, from the entodermal cyst with lymphoid wall, in which the carcinomatous infiltration of the cyst wall was just beginning, up to the larger growths infiltrating all of the cervical tissues. In the earlier stages in which the lymphoid tissue is persistent the histological picture resembles a lymph-gland with carcinoma infiltration, and there is no doubt that the so-called "primary carcinomas" of the lymph-glands of the cervical region were wholly or in part branchiogenic carcinoma. The appearance of a firm, non-fluctuating tumor in the branchial region of individuals over thirty-five should always excite a suspicion of branchiogenic carcinoma, and prompt operation should be carried out. Unless the tumor is removed in the early stages, the prognosis is very bad. I have seen some very pathetic cases of strong, healthy men in the forties developing "a swelling of the lymph-glands of the neck," operation without microscopical examination of the removed gland, then recurrence, often twice or thrice repeated removal before it occurred to the surgeon to have a microscopical examination of the removed tissue. Then the pathologist's diagnosis of branchiogenic carcinoma comes as a blow, its accuracy at first often disputed, and then a year or less of wretched and futile attempts at treatment with Coley's serum, Röntgen-ray treatment, etc., as after these repeated operations the condition becomes quickly inoperable, the cervical tissues becoming rapidly infiltrated, usually downward into the mediastinum and lungs. Secondary infection of the branchiogenic carcinoma is not rare, and the clinical picture may be confused, the process taken for a suppurative lymphadenitis, and the diagnosis possible only after microscopical examination. Routine examination of all "enlarged cervical glands" should be insisted upon by all wise surgeons, as the ultimate diagnosis rests alone upon the microscopic findings.

ALDRED SCOTT WARTHIN.

Brand, Ernst.—A German physician who owes his celebrity to the fact that he was the first to call the attention of the Profession to the value of cold water in the treatment of fevers, especially typhoid fever. He was born at Feuchtwangen in Franconia on January 2, 1827. He studied medicine at the University of Erlangen and received the degree of Doctor of Medicine from that institution in 1851. Not long afterward he settled in Stettin as a general practitioner, and in 1861 published his first paper on the cold-water treatment of typhoid fever. He died on March 7, 1897; but several years previous to his death, the title of Geheimer Sanitätsrat was conferred upon him in recognition of his valuable contribution to medical science.

Among his published writings the following deserve to receive special mention: "Die Hydrotherapie des Typhus," Stettin, 1861; "Die Heilung des Typhus," nebst dem Anhange: "Anweisung für die Krankenwärter bei der Behandlung des Typhus mit Bädern," Berlin, 1868; and "Die Wasserbehandlung der typhösen Fieber," Tübingen, 1877. (Pagel.) A. H. B.

FIG. 1087.—Ernst Brand.

Brandt, Thure.—Born in Södertelge, Sweden, February 6, 1819. As a Swedish military officer he went through a course of training at the Institute for Gymnastics in Stockholm. The idea of utilizing massage in the treatment of diseases of women first occurred to him while he was doing garrison duty at Norrköping, in 1847. Not being himself a physician he at first met with considerable opposition on the part of medical practitioners, but gradually, as the beneficial effects of the method became more and more manifest, this opposition was withdrawn, and the physicians eventually became his supporters. He died August 8, 1895. (Pagel.)

There seems to be no reasonable ground for withholding from Brandt the credit of having been the first to advocate the employment of massage for the cure or relief of affections of the pelvic organs. He published two papers on this subject, viz., "Uterinlidanden och prolapser," 1864; and "Nouvelle méthode gymnastique et magnétique pour le traitement des organes du bassin," 1888. A. H. B.

Braschysera.—An order of flies which contains some important families: *Muscidæ*, house fly, blow fly, flesh fly; *Œstridæ*, bot fly. A. S. P.

Brasdor, Pierre.—Born December 19, 1721, in a small village of the ancient province of Maine, France. His early studies in surgery were carried on in the city of Paris; and he made such rapid progress that he was able, in a comparatively short time, to give instruction in this department of knowledge to his fellow students. In 1752 he was appointed an *agrégé* in the College of Surgery, and afterward he was made, first, a full professor of anatomy, surgical operations, and general therapeutics, and then in turn counsellor of the standing committee, director, and vice-director of the Academy of Surgery. He died September 28, 1799. (Dict. Hist. de la Med.)

Brasdor was an experienced and skilful surgeon. He recommended, a long time in advance of Hunter, the treatment of aneurysm by the application of a ligature to the artery at a point between the tumor and the heart. He was also aware of the necessity, in certain cases, of applying a ligature to the artery on the distal side of the tumor; and he had learned that, in a few cases, ice might be applied with benefit. In addition to his acquirements in surgery, Brasdor had accumulated considerable experience in the veterinary art and, along with Tronchin and Bordeu, he was an ardent advocate of the practice of inoculation as a preventive of small-pox.

Of the few published writings left by Brasdor the following deserve to be mentioned: "Réflexions sur la fracture de la clavicule," in *Mémoires de l'Académie royale de Chirurgie*, vol. v., 1762; "Mémoire sur les amputations," *ibidem*, 1758; and "Mémoire sur la maladie épidémique des chiens," in *Mémoires de l'Academie royale des Sciences*, vol. vii. In Sabatier's *Médecine opératoire*, vol. iii., 1796, there is published a description of Brasdor's method of applying ligatures to polyps in the vault of the pharynx.

A. H. B.

Brashear, Walter.—Born in Maryland, in February, 1776. He commenced the practice of medicine at Bardstown, Kentucky, in 1806. In the same year he performed an amputation at the hip-joint, the earliest original surgical work of any magnitude ever done in the State. It proved to be the first operation of the kind in the United States. The result was a

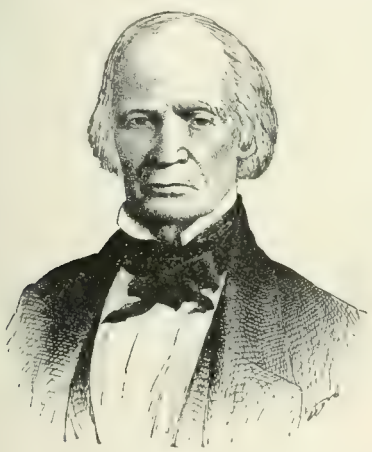

Fig. 1088.—Walter Brashear.

complete success. In 1813 he removed to Lexington, Kentucky, where he acquired an extensive surgical practice, devoting special attention to the diseases and injuries of the bones and joints. Later he abandoned medicine and became a sugar planter in Louisiana where he died at an advanced age. (A full and interesting sketch of the life of Walter Brashear will be found in Dr. D. W. Yandell's "Pioneer Surgery of Kentucky.") A. H. B.

Brass Founders' Ague.—See *Occupational Diseases.*

Braumia.—A genus of tapeworms. One species, *B. jassyensis*, is found in man. See *Cestoda.*

A. S. P.

von Braun, Carl.—Born in Fistersdorf, near Vienna, Austria, March 22, 1822. He received the degree of Doctor of Medicine in 1847. From 1849 to 1853 he acted as an assistant to Prof. Klein in his management of the Obstetrical Clinic—a clinic conducted in the Allgemeine Krankenhaus and designed primarily for the instruction of medical men. In 1853 he was appointed a "Privatdozent" in the University of Vienna, and very soon afterward he accepted a call to fill the regular chair of Obstetrics in Trent, Austrian Province of Tyrol. In 1856 he was invited to return to Vienna and occupy the same chair in that University. His appointment to the position of Rector of the University in 1868, the fact of his being knighted in 1872, and the further fact of his receiving the title of "Hofrat" in 1877—all these show how greatly esteemed Carl Braun was for the valuable services which he rendered as a teacher and for his high personal character. He died March 28, 1891. (Pagel.)

In addition to numerous contributions to current medical literature Braun published three larger books on obstetrical and gynecological matters, viz., "Klinik der Geburtshilfe und Gynaekologie" (in association with Chiari and Spaeth), Erlangen, 1855; "Lehrbuch der Geburtshilfe, mit Berücksichtigung der Puerperalprocesse und der Operationstechnik," Vienna, 1857; and "Lehrbuch der Gynaekologie," second edition, 1881. A. H. B.

von Braun, Gustav.—Born in Zistersdorf, Germany, on May 28, 1829. He was a younger brother of Carl Braun. He received his medical degree from the University of Vienna in 1853. After serving for three years as Assistant in the Obstetrical Clinic for Physicians he was made a Privatdozent in Midwifery in 1856. In 1862 he was called to the Joseph's Academy to fill the Chair of Obstetrics in that institution; and, when this organization ceased to exist in 1873, he was made professor and chief of the Second Obstetrical Clinic at the University of Vienna. From 1883 to 1884 he acted as Dean of the Medical Faculty. He retired from active teaching and practice in 1900. He died January 8, 1911.

Gustav Braun made a number of valuable contributions to medical literature. The titles of only a few of these may here be mentioned: "Operative Gynækologie and Geburtshilfe," Vienna, 1860; "Compendium der Geburtshilfe," Vienna, 1864 (2d edition in 1875); "Compendium der Kinderkrankheiten," Vienna, 1870; and "Lehrbuch der Geburtshilfe für Hebammen," 1894 A. H. B.

Brayera.—See *Cusso.*

Breast, Anatomy of the.—The breast is a prominence on the ventral surface of the body which in the female secretes the milk for the nourishment of the new-born. In the human species there are usually two of these eminences situated one on each side of the thorax. They are made up of the mammary glands and associate structures, that is, the true gland tissue, the stroma, and integument including nipple and areola. The term mammary gland is commonly, however, used as synonymous with breast.

The presence of mammary glands is one of the most prominent characteristics of that great class of the animal kingdom, the mammalia, where they first appear. Breslau from his study of the monotremes and marsupials is of the opinion that the mammary apparatus of the mammals is not essentially an entirely new development but has its origin in the so-called brood organ common to the progenitors of the mammalia. From these brood organs there is developed independently of one another the mammary apparatus of the monotremes on the one hand and of the marsupials and placentalials on the other. The mammæ are found in both male and female, but the size and development differ; the male gland as a rule remains throughout life in a rudimentary condition, while the female breast passes through

marked and important changes at puberty, at conception, after lactation, and at the menopause.

Embryology. In very early embryos, there is observed on either side a slight streak, running from the root of the stump-like fore-limb to the hind-limb, and situated a little behind and parallel to the membrana reuniens inferior. This is observed in rats of 2.5 to 5.25 millimeters (Henneberg) and in human embryos of from four to eight millimeters (Hirschland and Strahl), and was named by Schwalbe-Schmidt mammary streak (Milchstreifen). It is due to the cells of the ectoderm becoming deeper and more cubical.

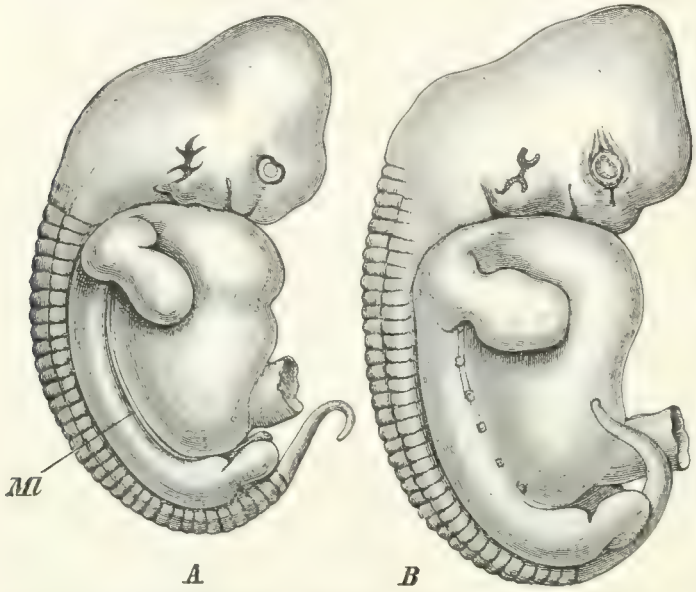

Fig. 1089.—*A*, Pig Embryo 1.5 cm. Long. *Ml*, Mammary line. *B*, Pig embryo 1.9 cm. long, with mammary hillocks. (O. Schultze.)

From the mammary streak there is soon produced, by multiplication of the cells, a well-marked ridge, the mammary line (Milchlinie or Milchleiste) (*Ml*, Fig. 1089, A). This well-marked microscopic ridge was first studied by O. Schultze in the pig, and more recently by Kallius, Stahl, Hirschland, and H. Schmitt in human embryos of about fifteen millimeters.

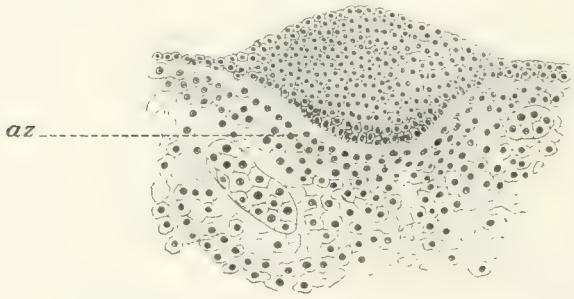

Fig. 1090.—Mammary Hillock of a Pig Embryo 1.5 cm. Long, with the Nipple Zone (*az*) becoming Differentiated.

In this line the epithelium develops more rapidly at certain spots, corresponding in situation to the future mammary glands of some animals and to the position where supernumerary mammæ occur in man. The line thus becomes moniliform, and finally isolated, spindle-shaped enlargements are produced by atrophy of the portion of the milk line lying between the enlargements (Fig. 1089, B). Thus the mammary hillocks ("Milchhügel") of Bonnet are produced (Fig. 1090). The projection of the line of hillocks, above the surface of the skin, is only very transient. In human embryos, toward the end of the second month of intrauterine life, the small tubercular thickenings, gradually increasing in size, become lens-shaped, and their convex surfaces project into the cutis, forming the mammary points (Milchpunkte). Large numbers of the mesodermic cells of the cutis collecting around the epithelial ingrowth form a condensed zone (nipple zone; *cf.* Fig. 1090), from which later the connective tissue and unstriped muscle of the nipple are developed.

The further growth results in flattening above with a projection of the deeper convexity of the lens, especially in the center. In this way there is produced a cone-shaped mass of the cells which sink deeper into the cutis.

Around the apex of the cone the greatest activity is manifest; the cells push deeper into the cutis, and spread out below to produce a large ball-like mass (body) connected with the surface by a narrow elongated part (neck; Fig. 1091). This is the so-called club-shaped stage.

There now appears on the free surface of the skin a small cavity, the "gland area" (Drüsenfeld of Huss), which soon deepens. In the formation of this not only the deep but also the superficial layer of the epithelium takes part. Around the border of the depression a ring-like ridge of cutis, the first rudiment of the areola, is raised up.

Upon the deep surface of the club-shaped mass, at about the twelfth week of intrauterine life, small bud-like masses of the epithelial cells appear (Fig. 1092). These rapidly increase in length, and force their way as solid plugs into the mesoderm beneath (Fig. 1093). This secondary epithelial development is the rudiment of the true secreting portion of the gland. The number of epithelial sprouts now seen (fifteen to twenty) corresponds with the number of excretory ducts which the mature glands will possess. The upper ends of the plugs are in the nipple zone, but the greater part of their lower ends project into the loose connective tissue of the cutis.

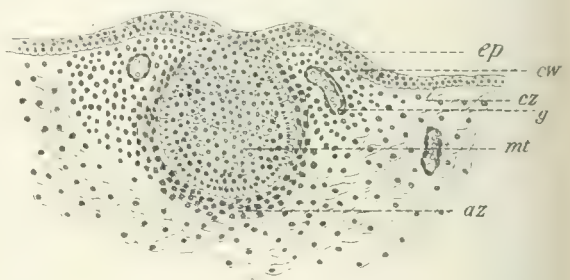

Fig. 1091.—Primitive Nipple, Club-shaped Stage of a Pig Embryo 6.5 cm. Long. *ep*, Epidermis; *cz*, layer of cylindrical cells; *cw*, cutis wall; *mt*, mammary point; *g*, blood-vessel; *az*, nipple zone.

Only some of these sprouts are held by Eggeling to represent the ducts of the mammary glands whose growth forms the parenchyma of the glands. Others are very early anlages of hair and still others anlages of sebaceous glands. Neither of these complete their development and become hair or sebaceous glands but join in the lactiferous duct.

There is now developed a new zone beneath the nipple zone, composed of young, round, closely packed connective-tissue cells. Surrounding and supporting the epithelial elements of the gland, these form the stroma of the gland (stroma zone).

A retrograde metamorphosis next begins in the central cells of the primary epithelial ingrowth, and from the center the degeneration proceeds peripherally and downward. It takes the form of a cornification (Fig. 1093, *hp*) and proceeds at first very rapidly, though its final progress is so slow that sometimes it is not complete until after birth. Ultimately it leads to the complete disappearance of the primary epithelial ingrowth or mammary point.

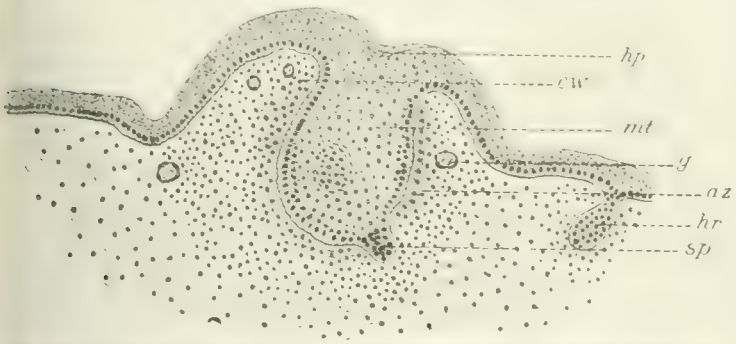

Fig. 1092.—Primitive Nipple of a 12 cm. Pig Embryo with an Epithelial Sprout *sp*. *cw*, Cutis wall; *mt*, mammary point. (For other letters, see Figs. 1090 and 1091.)

At the same time as the primary ingrowth is degenerating the secondary ingrowth, nipple zone, and stroma zone are continuing to develop. As the secondary epithelial plugs push their way into the underlying mesodermic stroma, they become clubbed below. At the same time the originally solid plugs are hollowed out and converted into tubes, and during the seventh month of intrauterine life, or about that time, give off numerous buds (Fig. 1093). In connection with these latter, small irregular groups of epithelial cells may be seen, the matrix of the acini. The branching of the ducts, even up to the time of birth, is but slightly advanced. At birth the milk ducts do not extend beyond the areola, and the whole gland shows an expansion of but one centimeter and weighs only thirty to sixty centigrams (Puech).

A rudimentary corpus mammæ is represented by a well-defined rounded mass, around the circumference of which the lobes project irregularly. The whole is embedded in a well-developed stroma, which is surrounded by fat lobules of the subcutaneous tissue. The coarse connective-tissue fibers of the stroma radiate from the corpus mammæ and become continuous with the fibrous capsules of the fat lobules. These latter surround but do not mix with the stroma. Beneath, the stroma is continuous with the fascia covering the pectoral muscle.

The fat layer of the skin becomes locally thickened in the region of the gland, but not until five or six years after birth does fat develop in the stroma between the gland lobules.

At birth the ducts possess a simple epithelium, cubical in the deeper parts, but cylindrical in the region of the nipple.

The time at which the various changes noted above occur varies considerably, being by no means constant. Even in the new-born the development is not always equally far advanced.

The nipple is developed in the human species toward the end of intrauterine life. Then the mesodermic tissue which constitutes the nipple zone rapidly increases, and between the elements smooth muscle cells soon appear. The center of the originally depressed gland area becomes situated upon the tip of a cone-shaped projection. The exact time of the elevation of the nipple varies; sometimes it occurs in embryonic life; yet frequently in children of from ten to twelve years the depressed gland area with its surrounding wall still persists.

There has been considerable difference of opinion as to whether the mammary glands were related to the sebaceous or the sweat glands. All recent investigations would lead us to favor the Benda-Eggeling theory of their relation embryologically to the sweat glands. They not only resemble the sweat glands developmentally but functionally; most modern investigators believe the milk to be a secretion similar to that of the sweat glands. Structurally also Eggeling describes in both mammary and sweat glands groups of more or less round cells while the hairs and sebaceous glands present a peripheral zone of cylindrical cells.

Upon the areola, sebaceous and sweat glands are developed. Rein has shown that the enlarged sebaceous glands of the areola (tubercles of Montgomery) are accessory rudimentary milk glands.

Condition at Birth.—It will be seen that the new-born of both sexes possess all the skin ingredients of the gland, and moreover the gland can secrete milk,

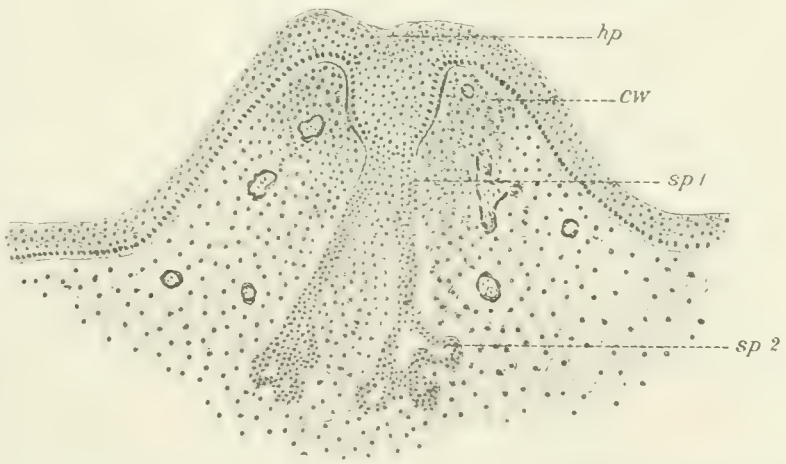

Fig. 1093.—Nipple of a 20 cm. Female Pig Embryo. The epithelial sprouts, excretory ducts *sp* 1, have near their terminal end a lumen; secondary sprouts (*sp* 2) are also seen; *hp*, cornification of the epithelium is beginning.

which is called in German "Hexenmilch" (witches' milk). This occurs from the fourth to the tenth day after birth, and is accompanied by a swelling of the gland. It has been shown by Rein and others to be true milk. According to De Sinéty considerable changes take place in these first ten days, after which there is some acinous tissue resembling that which is

seen in the adult. But only the main ducts are excavated. Bizzozero and Ottolenghi state that Hexenmilch consists of, 1. milk drops of various sizes; 2. leucocytes, unchanged or containing little fat drops; 3. milk bodies in which the existence of the nucleus may be shown; 4. mulberry-like groups of milk drops rolled together with one nucleus; 5. typical colostrum corpuscles. It has been shown by Benda that it is only the lumen of the acini of the child's gland that contains fat, the cells do not.

From birth till puberty the breasts remain rudimentary, simply keeping pace with the general body growth. The intralobular ducts and beginning of the acini remain solid, and though there are some slight changes, such as the development of a few acini buds, yet the condition found shortly after birth persists almost unchanged.

Changes at Puberty.—In the female at puberty an abrupt change like that affecting the entire organism takes place. This consists in further branching and growth of tubes into the surrounding tissue, and also the further development of the stroma. The fat which appeared in the stroma at the fifth to the sixth year rapidly increases in amount. Now development proceeds rapidly, but there is no distinct subdivision into the lobules, the true secreting acini being few in number. At each succeeding menstrual period a slight engorgement occurs, and it is probable that it is accompanied by increased development. At these times slight pricking sensations and pain may be felt, and in some cases a yellow secretion is expelled. Soon after puberty the breasts become very well developed, but they consist mainly of fatty stroma and excretory ducts, with a relatively small amount of glandular tissue.

In the male at puberty there is sometimes a slight swelling of the gland which may also become somewhat harder and sore or painful. This disappears after a short time and no further change, as a rule, occurs in the male breast.

Situation.—The breasts are situated in the subcutaneous tela, superficial to the pectoral muscles; as usually described they are said to extend from the

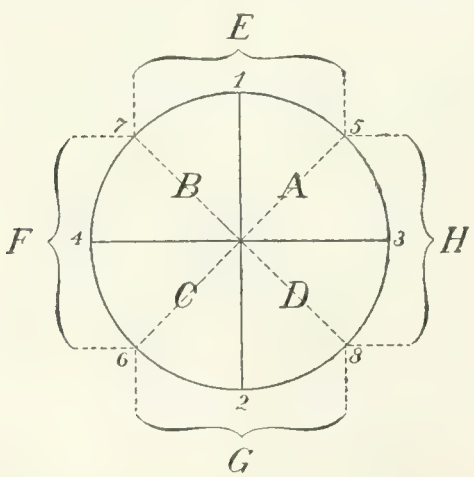

Fig. 1094.—Diagram to Show Method of Dividing Breasts for the Purpose of Description. 1 to 8, Lines of division for the location of the different sections (see text). *A*, Mesocephalic; *B*, cephalolateral; *C*, caudo-lateral; *D*, mesocaudal; *E*, cephalic; *F*, lateral; *G*, caudal; *H*, mesal sections or divisions.

second or third to the fifth, sixth, or seventh rib, and from the edge of the sternum to the ventral fold of the axilla. These estimations are undoubtedly based upon external conformation, and of necessity, therefore, refer only to those portions of the gland which cause its projection above the surrounding surface.

Stiles, from his examination of breasts before and after operation, has found that the usual description takes no account of the peripheral processes, which extend in the subcutaneous tissue, often far beyond the prescribed limit. Moreover, he has shown that this holds true for nulliparæ, as well as for multiparæ, though of course the processes are much more marked in the latter.

He divides the breast by two intersecting lines, a vertical (1–2) and a horizontal (3–4), into four segments (Fig. 1094), named respectively cephalomesal, cephalolateral, caudolateral, and caudomesal. For purposes of more careful description, a second division is made by two oblique lines (5–6), and (7–8) into four other segments, cephalic, lateral, caudal, and mesal.

The vertical diameter (1–2) extends from the caudal border of the second rib to the sixth costocartilage where it begins to sweep cephalad toward the sternum. The horizontal (3–4) begins opposite the fourth rib or fourth interspace, just within the lateral border of the sternum, and extends to the mid-axillary line at the level of the fifth rib or fifth interspace. The oblique line (5–6) extends from the cephalic border of the third costocartilage, a little lateral to the border of the sternum, to the seventh rib a little ventral to the mid-axillary line. The oblique line (7–8) begins on the third rib a little lateral to the ventral axillary fold, and extends to the sixth costocartilage midway between its angle and sternal end. The circumference connects the extremities of the lines.

When the arm is raised, as for operation, the nipple, in nulliparæ, is opposite the fourth rib or fourth interspace and 2.5 centimeters mesad to the axillary border of the pectoralis major. Thus the extent to which the breast overlaps the border of the pectoralis major is considerable. The level varies with the stature; as a rule in tall women the breast is more caudal, while with short and broad-chested women it is more cephalic in position.

Relations.—The relations of the dorsal surface of the breast can best be treated by describing each segment separately.

The mesocephalic segment (Fig. 1094, A) rests entirely upon the pectoralis major muscle; so also does the mesocaudal segment (D), except at its caudal edge where it overlaps the aponeurosis of the external oblique muscle.

The cephalic half of the cephalolateral segment (B) rests upon the pectoralis major muscle, the edge of the pectoralis minor muscle, and for a slight extent upon the serratus magnus muscle. Upon the latter and under cover of the pectoralis major it extends up into the axilla as far as the third rib. This forms the so-called axillary tail of Spence. The circumference of this segment crosses the border of the pectoralis major muscle, where its fibers leave the third rib to form the ventral axillary fold.

The caudal half of the cephalolateral segment (B) and the cephalic half of the caudolateral (C), with the exception of a small portion near the nipple which is superficial to the pectoralis major muscle, lie upon the serratus magnus muscle. The caudal half of the caudolateral segment (C) overlies those portions of the external oblique and serratus magnus muscles which arise from the fifth and sixth ribs, except a portion near the nipple which is over the pectoralis major muscle.

Thus it will be seen that, with the arm in the position assumed for operation, fully one-third of the whole breast lies caudolateral to the axillary border of the pectoralis major muscle. One-half of this overlies the axilla, filled with its fatty fascia containing numerous lymph nodes. Some of these lymph

nodes appear to be in direct contact with the breast tissue.

The dorsal surface of the breast is concave, composed mainly of stroma containing projecting processes of the parenchyma. The stroma is continuous with a loosely interlaced network of connective tissue which forms the pectoral fascia. This fascia forms the sheath for the pectoralis major muscle and like the sheath of all muscles sends numerous septa through the muscle binding together the muscle bundles. It is quite thin and it is difficult to separate it from the muscle, particularly in spare subjects. In some it attaches the gland so closely to the subjacent muscle that movement of the arm

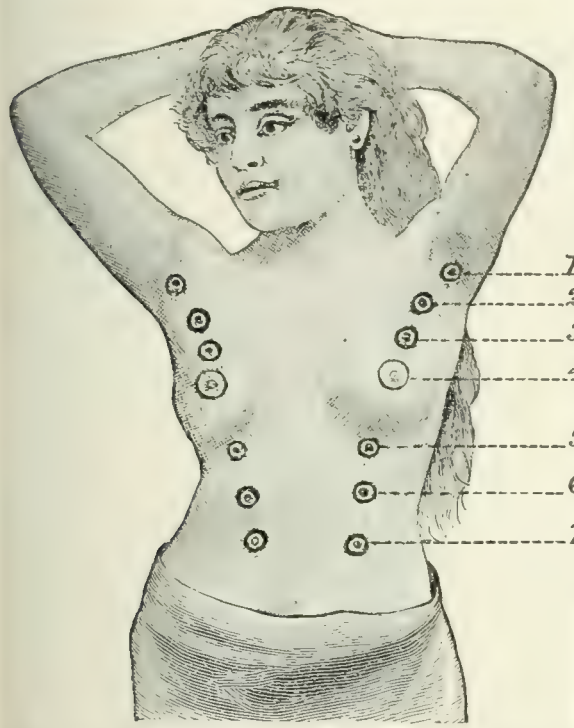

Fig. 1095.—Diagram Showing the Mammary Arrangement of Man's Early Progenitors. (Williams.)

causes considerable movement of the gland. In others it is very loose, but even with these some movement is observed when the arm is raised. In these latter cases loose areolar tissue spaces have been described by Chassaignac as serous bursæ (sub- or retromammary bursæ).

Close examination has shown that the portions of the parenchyma which project into the stroma of the dorsal surface send numerous minute processes into the retromammary connective tissue. Some of these even accompany the septa of the pectoral fascia between the muscle fibers.

The anterior surface is for the most part smooth and convex. It is covered with skin continuous with that of the surrounding surface. The skin is thin and delicate and differs from that of the ventral surface of the body only at its center, where the raised and pigmented areola surmounted by the nipple is seen.

The circumference, although in the main circular, is very irregular owing to the processes of the parenchyma. There are usually three fairly well-marked cusps. The largest projects toward the cephalic part of the axilla and has been already referred to as the axillary tail; another, much smaller, extends toward the caudal part of the axilla; the third reaches toward the sternum.

These irregularities are not apparent upon the surface of the body where the caudal border of the circumference of the breast is distinctly marked off from the surrounding parts by a furrow, but slightly marked in young thin nulliparæ, more marked in fat women, and especially prominent in multiparæ; on the other hand, the cephalic border of the circumference is as a rule ill-defined, the breast arising in a gentle slope from the surrounding tissue.

Shape.—In the female Hoerschelmann distinguishes four stages in the development; first, the neutral or puerile with disc-shaped papillary area around the nipple; second, the half globular nipple area and nipple form with the real or primary mamma completely wanting; third, the primary mamma stage with half globular form of nipple and area around it; fourth, the primary mamma with discoidal nipple area and prominent nipple. In the male the development proceeds little beyond the neutral stage.

Well nourished adult females should possess a hemispherical or conical breast with smooth surface, while emaciated subjects as a rule present a flat discoidal breast with irregular surface. In adult nulliparæ (Figs. 1098 and 1099) it is somewhat conical, due to the relatively large amount of gland substance compared with the stroma. In stout subjects the relatively greater amount of circummammary fat produces a hemispherical breast. After lactation it frequently becomes pendulous, a very marked sulcus being produced between the breast and the surface of the thorax. This is due to the atrophic fatty changes which at this time affect the secreting structure and produce a flabby condition. We may distinguish three principal types: 1. Standing, up to and during fullest development; 2. drooping, after full development; 3. hanging, may reach down below the border of the ribs. In these cases the breast sometimes becomes almost cylindrical in shape. Rarely the attachment of the breast to the thoracic wall is contracted, producing a stalk. This is the pedunculated breast.

Consistence.—The well-developed breast in the virgin and nullipara is hard, firm and elastic. It loses its consistency after having attained full activity, especially if there has been a period of nursing. In women who have had several children the breasts are as a rule soft and flabby, overhanging their attachment to the thoracic wall to a greater or less extent.

Weight.—In the adult nullipara the breast weighs from 140 to 200 grams; in nursing women from 400 to 500 and in exceptional cases as much as 900 grams.

Number.—A single pair of breasts is the least number normally found in any mammal. This is the usual number in man, as also in apes and a few other animals. The largest number is found in certain of the insectivora, in whom there are as many as eleven pairs. Between these limits all gradations exist. Reduction of this number is very exceptional, but there are numerous cases on record of supernumerary breasts.

Arrest may occur in their development at any time; when it occurs very early in embryonic life the breast is entirely suppressed (amazia). This is extremely rare in the human subject, and is frequently associated with other defects in development. Williams finds complete absence of both breasts one of the rarest anomalies; outside those occurring in acephalic monsters with deficient chest walls, only four cases are recorded in literature. Complete absence of one breast is slightly less rare. Recently Wayte has re-

ported the absence of the right breast in a male whose father also had the same defect. A more frequent condition is the arrest of development at a later stage leading to rudimentary but functionless organs (micromazia). This also may affect one or both sides, and as with amazia may or may not be associated with deficiences in the sexual organs or chest wall.

Absence of the nipple (athelia) is much commoner than the above. Williams has pointed out that in these cases there is really no absence of nipple structures, but simply a failure of the embryonic gland area to become elevated. This is usually unaccompanied by other anomalies, and generally affects both breasts. The areola is rarely absent when the nipple is well developed, but with athelia the areola may be absent or slightly formed. Intermediate conditions between complete absence and the perfect nipple, due to degrees of elevation of the embryonic gland area, produce the various recorded congenital imperfections.

In the development of supernumerary mammæ it would seem that we have a most excellent example of atavism since a study of the comparative anatomy of the mammary gland shows that the progenitors of man have more than one pair of mammæ. The lemurs for example, while having only one pair of glands functional, possess rudimentary abdominal and inguinal mammæ and an examination of other species shows that the number of glands is being gradually reduced.

The theory presented by Hugo Schmidt, that supernumerary mammary glands and nipples represent some of the line of ordinarily temporary epithelial thickenings, mammary hillocks, which have persisted and undergone further development, is most generally accepted. Walter has recently questioned this on the ground that the number of mammary hillocks, forty in some embryos, greatly exceeds the number of mammæ found in any known species. On a number of grounds he has suggested that the epithelial thickenings of H. Schmidt might represent not the anlage of the mammary glands but of the marsupial pockets which Bresslau has shown to precede the development of the milk point in the marsupials. The number would, however, remain the same and therefore I cannot see that his explanation is any more helpful. It would seem almost certain that supernumerary mammary glands and nipples have as their anlage some of these early epithelial growths.

By a careful study of all recorded cases Williams found that the position occupied by the mammæ in lower animals and by the mammary hillocks in embryos was the same as that occupied by aberrant mammæ. He considers that man's early progenitors were possessors of seven pairs of breasts (Fig. 1095), three cephalolateral to the normal, and three caudomesal to them.

First pair—in the pit of the axilla.

Second pair—in the middle of the ventroaxillary border.

Third pair—just cephalad and slightly laterad of the normal pair.

Fourth pair—the normal mammæ.

Fifth pair—just caudad and slightly mesad of the normal pair.

Sixth pair—caudad and slightly mesad of the preceding, near the costal margin.

Seventh pair—caudad and slightly mesad of the preceding, on the upper part of the abdomen.

Out of 166 cases collected by Leichtenstern and Bruce, there were only 4, 2.41 per cent., which could not be assigned to one or another of these positions. These mammæ erraticæ are supposed to be due to reversion to the ancestral characters much more remote than those given above.

The following table of 105 cases recorded by Leichtenstern shows the relative positions of the accessory mammæ. On the anterior side of the thorax, 96 cases (91 per cent.); in the axilla, 5 cases (4.7 per cent.); on the back, 2 cases; over the acromion, 1 case; over the outer side of the hip, 1 case. Of those on the anterior side of the thorax 94 per cent. were developed caudad to the normal pair and in a converging position.

Supernumerary mammæ are represented often only by a nipple, which may or may not be surrounded by an areola (true polythelia); or the duct of the gland may open upon the surface by one or more openings, no nipple or areola being present; or there may be no communication with the surface whatever. Rarely the extra gland is perfectly developed and functional.

Rudimentary breasts cephalad to the normal ones are rare—but 12 out of 166 cases, or 7.2 per cent. Abdominal mammæ are very rare. In polymazia the normal pectoral mammæ are always present in their proper position and well developed. Of Leichtenstern and Bruce's 166 cases, there was only a single extra structure in 112, or 67.4 per cent.

Numerous records of supernumerary mammæ or nipples are found in literature. The condition is much more common than previously supposed. Bruce found in 315 individuals, of both sexes taken indiscriminately, polymastism in 7.6 per cent.; in 207 males 9.1 per cent., and in 104 females 4.8 per cent.

Out of 2,189 men recruited in the military district of Donaueschingen 62 were found with one supernumerary teat and 4 with two—that is, 1 case in about every 33, or a little over 3 per cent. Besides, 48 others were found who showed discrete pigmented patches symmetrically placed upon the line usually occupied by supernumerary mammæ or nipples. These represented small areolæ.

In the course of physical examinations made on 2,561 students at the Cornell University Gymnasium, Hathaway found 21 cases or 0.82 per cent. in which supernumerary nipples occurred. In two of the cases the nipples were paired. In only two of the cases was the extra nipple cephalad to the normal nipple.

Supernumerary mammæ are found more often on the left than on the right side. So also in amazia, the right mamma is absent more frequently than the left.

Anomalies arising late in the developmental process lead to two nipples on one areola (intraareolar polythelia); or two on one breast (intramammary polythelia).

Supernumerary mammæ or nipples are probably found in all races. They have been noted by Owen in the orang and by various observers in many animals. Supernumerary mammæ appear often to be hereditary. In 7 out of 92 of Leichtenstern's cases, or 7.6 per cent., there was a history of such condition in near relatives. The condition is not usually associated with other malformations.

Although it is generally believed that women with more than one breast are no more liable than other women to bear twins, Teizo Iwai from his study of Japanese women believes that there is probably a relation between polymastia and multiparous births. He believes also that those who have supernumerary mammary glands have a tendency to become more frequently pregnant and also points to the fact that our progenitors were far more fertile than the race to-day. In this connection Bresslau emphasizes the view of Bonner that supernumerary nipples and other mammary organs are remains of an originally (primitive) greater number of mammary glands, which number has been reduced in the course of development, and not that they are resulting structures of increasing fertility.

Size and Volume.—The breast, which at birth measures but ten millimeters in diameter, increases but little until after puberty, when it rapidly attains

a diameter of 100–130 millimeters and a thickness of 50–60 millimeters. The greatest length is parallel to the border of the pectoralis major.

Soon after impregnation it again increases in volume, and although it decreases somewhat at the fourth or fifth month, it becomes greatly enlarged again at the end of gestation. The second or third day after delivery the milk begins to be secreted, and now the true functional activity of the gland is first established. The milk accumulates in the alveoli and in the excretory ducts. The gland becomes harder, heavier, and more voluminous. It soon acquires a volume two or three times that of the gland before pregnancy.

After lactation it returns again to its ordinary size, which it retains until another pregnancy and another period of activity. It is now less smooth, firm, and elastic than the virgin mamma.

After the menopause the useless gland with the rest of the genitals becomes atrophied. The glandular and secreting structures are frequently replaced by fat, when but little reduction in size occurs. In other cases the fat does not replace the gland tissue but the entire gland is reduced to a small fibrous area around the nipple and immediately beneath the skin. Thus it returns at last to a condition approaching the infantile.

The two breasts are seldom equal in size, the left usually being the larger, sometimes quite considerably. This is thought to be due to the fact that most women are right handed and therefore nourish the child more on the left side.

The size of the breasts presents considerable ethnological variations. Huschke says that, as a rule, they are more voluminous in warm than in cold countries, and in moist countries and in valleys than in dry countries and mountains. As regards races, variations are considerable, the people of southern Africa being remarkable for their large and pendent breasts.

In individuals, the size of the breast offers considerable variations. It appears that the development is independent of the build and constitution; large, robust women are frequently seen with very poorly developed breasts, while, on the other hand, small women are seen with large, well-formed breasts.

Fig. 1096.—A Part of the Ventral Surface of the Corpus Mammæ, Showing the Branchings of Two Milk Ducts. (Henle.)

The mammæ are formed of stroma containing fat and the essential gland structure. It is therefore clear that size alone will not determine the activity of the gland. A breast may be formed of a maximum amount of stroma and a minimum amount of parenchyma (fatty mammæ), or of a maximum amount of gland tissue and a minimum amount of fat (glandular mammæ). For this reason large breasts may furnish very considerably less milk than much smaller ones.

De Sinéty has pointed out that city-bred women are likely to have breasts much more poorly developed and functionally less active than their country sisters. This he attributes to the social conditions in the city leading so often to the wet-nurse and bottle, and he believes that this, carried through several generations, has led to an inherited characteristic. Thus the breast is following the law of morphology, that those organs which have become functionless and useless gradually are less and less developed and finally disappear.

Structure.—The breasts are composed essentially of three parts: first, the mammæ proper; second, the covering skin; third, the surrounding fatty tissue.

The mammæ, like all glands, consist of two parts: the parenchyma, and the stroma. The latter includes the fat, which is embedded in it, also the blood-vessels, lymphatics, and nerves, which ramify through it.

Parenchyma.—The parenchyma is divided into a central compact part, the body or corpus mammæ,

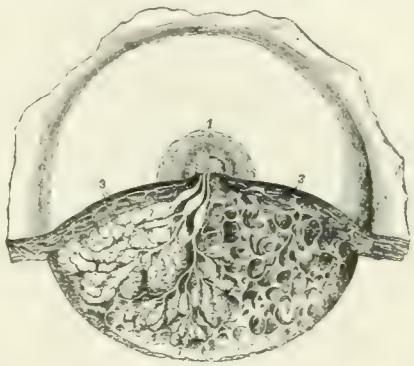

Fig. 1097.—Dissection of the Lower Half of the Female Mamma during the Period of Lactation. (Luschka.) *a*, *a*, *a*, Undissected part of the mamma; 1, the mammilla; 2, areola; 3, subcutaneous masses of fat; 5, three lactiferous ducts passing toward the mammilla where they open; 6, one of the sinuses or ampullæ; 7, some of the glandular lobules which have been unravelled; 7′, others massed together. (Quain.)

surrounded by peripheral processes. It is made up of lobes (lobi mammæ) divided into lobules (lobuli mammæ). All of the lobules of a lobe empty by small ducts into larger ones. These ultimately lead to one large lactiferous duct, which opens upon the nipple (Figs. 1096 and 1097).

When the covering parts are removed, the gland presents a flattened mass with an irregular, circular outline, thicker in the center than at the periphery. The ventral surface is convex but quite uneven, due to the processes which project toward the skin. The thick central portion mentioned above is the *corpus mammæ*, and upon the size and extent of this the external conformation of the breast depends. The dorsal surface, as already noted, is flat or slightly concave and much less irregular than the ventral surface (Figs. 1098 and 1099).

The circumference is quite thick and well defined, but it is thicker caudad than cephalad (Fig. 1098). When a section is made through the gland at the level of the nipple, the cut surface of the corpus mammæ appears triangular. The apex of the triangle is at the nipple, and the base, which represents the dorsal surface, rests against the thorax, from which it is separated by the stratum of loose areolar tissue.

Extending from this central compact area of glandular tissue, the peripheral processes reach in all directions. As already noted, there are three main cusps: one extends cephalad toward and into the axilla; another caudad of the axilla; while the third reaches toward the sternum. Besides these large processes there are numerous small ones, which

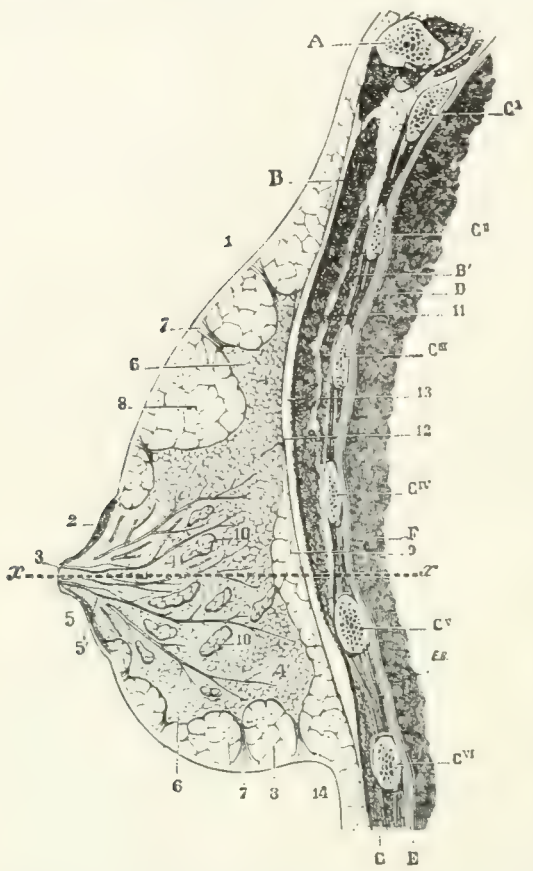

Fig. 1098.—Vertical Ventrodorsal Frozen Section of the Right Breast of a Woman, Twenty-two Years Old. C1–C6, First to sixth ribs; A, clavicle; B, pectoralis major; B', pectoralis minor; C, external oblique; D, intercostals; E, pleura; F, lungs; 1, skin of breast; 2, areola; 3, nipple; 4, mammary gland, central part; 4', peripheral part; 5, milk ducts; 5', sinus; 6, cusps of the mammary gland; 7, ligaments of Cooper, continued to the skin; 8, fat lobules; 9, fatty retromammary pad; 10, intramammary fat; 11, aponeurosis of pectoralis major; 12, superficial fascia forming suspensory ligament of breast; 13, layer of loose areolar tissue between superficial fascia and subjacent serous aponeurosis of the breast; 14, submammary furrow. (Testut.)

radiate in all directions around the circumference. These form numerous branched, interlacing processes enclosing and surrounding masses of fat.

From the ventral surface triangular processes project toward the skin (7, Figs. 1098 and 1099), and from the apex of the triangle the connective tissue covering the gland is prolonged to the dermis. In thin women the parenchyma at these points reaches almost to the surface.

From the dorsal surface, much more delicate processes project into the retromammary tissue, even reaching through this and extending into the pectoral fascia to get between the fiber bundles of the pectoralis major muscle. These processes are very minute and are often overlooked.

The relative amount of parenchyma to the stroma varies in different nulliparæ, also even in the same breast one lobe or section may have numerous well-developed lobules, while another has few or none, these remaining almost as at puberty merely branching ducts. The parenchyma, on close naked-eye inspection of a cut surface of fresh gland, is seen to be made up of closely packed sago-like grains.

Ducts.—The ducts are also seen in a cross-section, running through the nipple to its summit, where they open. Arising from the acini the minute ducts unite to form larger canals, so that each lobule gives rise to a single lobular duct (Fig. 1097). These join to form larger and larger ducts until but one duct leaves each lobe. This is known as the galactophorous or *lactiferous duct*. These, fifteen to twenty in number, corresponding to the lobes of the gland, gather at the nipple, through which they pass, in a vertical direction, to open upon its summit. Beneath the areola, each duct presents an irregular, fusiform swelling twelve to fifteen millimeters long and six to eight millimeters wide, known as the ampulla *lactiferous sinus* (Fig. 1097), also as the sacculus or reservoir. Secondary ampullæ occur here and there on the ducts. In the ampulla and the large ducts, milk accumulates in the intervals between nursing. Ectal or superficial to the sinus, the ducts are reduced in size and collected into a bundle, the largest ones occupying the center. Side by side, surrounded by muscle, areolar tissue, and vessels, and without communicating, they pass to the summit of the nipple. Here separately by minute orifices, they open into the bottom of depressions. The orifices, which measure six millimeters are distinctly smaller than the ducts. In the loose areolar tissue under the areola, the ducts and sinuses receive additional minute tributaries from the small adjacent lobules.

The ducts are composed of two coats, an external and an internal. The external coat is formed of white fibrous tissue intermixed with longitudinal and circular elastic fibers. Smooth muscle fibers have also been described. They are said to be particularly abundant around the ampullæ, where they form an imperfect sheath. The inner coat is formed of epithelium resting on a basement membrane. The epithelial cells, constituting a single layer, are flat in the lobular ducts, becoming cubical in the larger ducts, and columnar in the lactiferous ducts and ampullæ.

Lobes and Lobules.—Each of the fifteen to twenty ducts is the outlet for a single mammary lobe. Each lobe is of a reddish cream color and rather friable, and is a compound tuboracemose gland. Although each lobe is in contact on either side with the neighboring lobes, there is no known communication between them. The lobes are separated, by a considerable amount of areolar tissue, into a number of subdivisions, *mammary lobules*, which in turn are made up of acini (Fig. 1097).

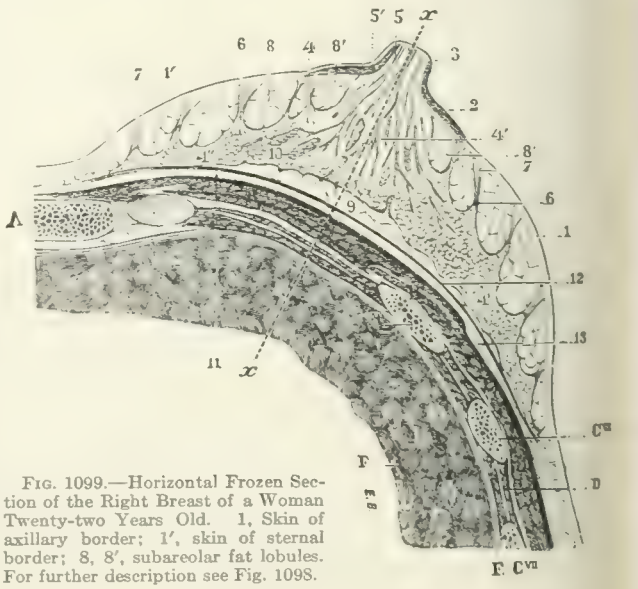

Fig. 1099.—Horizontal Frozen Section of the Right Breast of a Woman Twenty-two Years Old. 1, Skin of axillary border; 1', skin of sternal border; 8, 8', subareolar fat lobules. For further description see Fig. 1098.

Acini. The acini are small, spherical, or pyriform masses, measuring on an average 0.13 to 0.15 millimeter in diameter. An acinus consists of a minute sac lined by a single layer of small granular epithelial cells (Figs. 1100 and 1101) resting on a delicate hyaline membrana propria. This latter completely envelops the acinus, and is continued for a short distance on the minute excretory duct, with which the acinus connects. The above is the condition in a gland which has not yet become active. Brouha believes that the gland acini is lined by a double layer of epithelial cells and that there is no membrana propria which is only an automatic formation. The inner layer of cells monopolizes the secretory activity.

Fig. 1100.—Terminal Branches of a Milk Duct from the Breast of a Young Woman. (Bardeleben, × 56.)

Up to the time of pregnancy the breast consists, as already pointed out, almost exclusively of stroma and excretory ducts, with a relatively small number of acini. These with the beginning of lactation enlarge, and become distended with a clear, slightly viscid yellowish secretion (Fig. 1101). Their cells are flattened against the membrana propria, and contain fat globules of varying sizes.

The fluid in the acini at this time is the colostrum. It is produced for the first two to three days after delivery, until the free secretion of milk is first established. It contains a lager percentage of albumin and globulin and a smaller percentage of milk sugar than normal milk.

Besides serous fluid, colostrum is composed of fat globules of varying size, similar to those found in normal milk but somewhat larger and having a tendency to agglutination; also of granular cells, spherical or oval in shape, having a diameter of from three to twenty-five μ (colostrum corpuscles). The corpuscles consist of a mass of fat globules surrounded by protoplasm.

There appears to be still much controversy as to the origin of the colostrum corpuscles. Rauber considers them leucocytes that have wandered into the alveoli and undergone fatty degeneration, Bizzozero and Vassale believe that they are leucocytes whose main function is to absorb in the lumen everything which is left unworked, Czerny believes that they are leucocytes which are gradually filling with fat. Others believe that the central cells of the acini take up fat or degenerate and form the colostrum corpuscles.

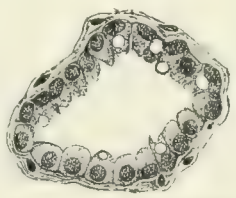

Fig. 1101.—Mammary Gland of the Dog. Transverse section of a terminal vesicle, showing an early stage of the formation of fat globules. (Heidenhain.)

Colostrum corpuscles are also supposed to be found in milk when the gland is not secreting completely or when its secretion has been interfered with.

When fully active the acini secrete true milk. The protoplasm in the cells becomes displaced toward the periphery by the accumulation of oil drops (Figs. 1102 and 1104). The minute oil drops, at first separate, become confluent, forming larger globules which occupy the greater part of the entire cell.

There is considerable difference of opinion as to just how the milk is secreted. There are five theories of milk secretion which have been held by noted investigators: 1. The necrobiosis theory, where the cells are spontaneously worn out and cast off, supported by Virchow but abandoned in 1871; 2. the pure secretion theory advocated by Kehver, Sanger, Schmidt, Bizzozero and Vassale, Benda, Unger, Ottolenghi, and Bresslau; 3. the leucocyte theory of Rauber, which had no other followers; 4. the partial necrobiosis theory, necrobiosis followed by decapitation of the secreting cells and the formation of new cells out of their basement membrane, supported by Partch, Heidenhain, Nissen, Frommell, Steinhous, Duclert, Limon and Bertkan; 5. the mixed theory, transitory partial necrobiosis, then pure secretion proposed by Michaelis and supported recently by Brouha. The questions at issue then are whether the fat is formed as a secretion of the cell or by the degeneration of its protoplasm and whether it is liberated from the cell by rupture and destruction of the entire cell or only part of the cell or as a pure secretion; whether the nuclei found in the milk are derived from the degenerated epithelial cells or from the leucocytes.

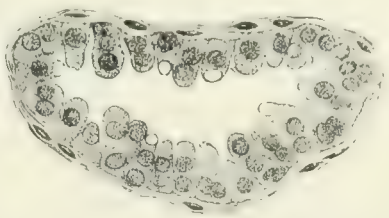

Fig. 1102.—The same Anatomical Relations as are shown in Fig. 1101. The gland, however, is in its highest stage of functional activity. (Heidenhain.)

It is quite certain that the milk sugar and protein of the milk are the products of pure secretion and it seems altogether probable to the writer that the fat also is produced in this way. Some of the gland cells are of course worn out during the course of the secretory activity and are cast off to be replaced by new ones. The gland cells are thought by some to be replaced by karyokinesis of the active cells remaining *in situ;* by others to arise from a deeper layer of cells; still others believe they arise by amitosis.

Fig. 1103.—From a Cross Section of the Corpus Mammæ of a Woman who Died during Childbirth, showing the Cubical Epithelium of the Tubules. (Bardeleben, × 116.)

Within an acinus the cells are cubical, or even columnar and of very unequal size. Some are found large, distended, with fat projecting into the lumen, others small, consisting merely of a nucleus and so little fat that it is obscured by the protoplasm. Between these are all grades.

During lactation the acini have a comparatively wide lumen, the epithelial layer forming but a thin lining to the irregular tubular or spherical spaces.

At all times there are numbers of mast cells in the connective tissue surrounding the lobules. During

lactation these are immensely increased. They have been supposed to have some connection with the secretion of the milk, but their exact function is not yet known.

The milk which distends the acini during full functional activity consists of fat droplets which were present in the cells, floating in a clear albuminous fluid (milk plasma). The minute milk globules vary, are from 2 to 5 μ in diameter and occasionally larger. They do not coalesce because they are probably, though this is disputed by some, surrounded by a delicate sheath of casein, Acherson's membrane.

During pregnancy and lactation, the increase in the size of the gland is due largely to increase of the parenchyma. This consists of an increase in the size and number of the lobules. Finally they increase so much that they touch and cause a disappearance of fat between them. At this time on section the naked-eye appearance closely resembles that of a salivary gland.

Fig. 1104.—Transection of a Tubule of the Corpus Mammæ. *Ep*, Glandular epithelium; in the lumen are milk globules, *Mi*, and colostrum corpuscles, *Col*. (Bardeleben, × 400.)

Moreover, at this time the superficial fat becomes absorbed, and the vessels become dilated and their walls thickened. The breast, due to the rapidly growing acini, presents to the hand an uneven feeling. The acini increase first on the peripheral processes, thence along the larger ducts toward the center of the corpus mammæ. While some parts of the gland are at the height of their activity others are in a resting condition and later these probably become quiescent while the others are active.

Practically nothing is as yet known in regard to what stimulates the mammary gland to develop at puberty. We have also almost no knowledge of the agency by which the gland is stimulated to growth at conception and in late pregnancy to produce scanty colostrum. After delivery there is apparently still another stimulus which causes the gland to secrete colostrum quite freely for a few days and then the true milk. It is almost certain that the uterus and the ovaries have some influence on the development of the glands and on the secretion of milk. Whether the uterus and ovaries act upon the mammary gland through their effect upon the specific secretory nerves of the gland or by their effect upon the vasomotor nerves of the blood-vessels supplying the glands or through an internal secretion acting through the vascular system is not certainly known. There is most likely a direct action of the central nervous system upon the secretion and it is altogether probable that both the other influences are more or less active in causing the development and secretion of the mammary glands. The experiments of Lane-Claypon and Starling seem to prove that there is produced in the body of the fetus a substance, in the nature of a harmone, which causes the mammary gland to develop but inhibits its secretory activity. They injected into a virgin rabbit extracts of fetuses and caused a development of mammary glands very like those normally developed after pregnancy. Extracts of uterus, ovary and placenta had no such effect.

The secretion when formed distends the acini and smaller ducts and finally the lactiferous ducts and sinuses. When these are distended the secretion ceases. When the tension is relieved by emptying the ducts whether by the suckling young or by some other means, the secretion is reestablished. Whether the secretion is inhibited by direct pressure on the cells or reflexly is not known.

After lactation the breast returns to a resting stage. The parenchyma undergoes revolution, and fat is developed in the stroma. The acini are reduced to narrow tubules, many becoming atrophied. The gland does not regain its virgin appearance; therefore it is easy to tell an involuted multiparous from a nulliparous breast since the corpus mammæ is loose, irregularly broken up, and less distinct, and the peripheral processes are larger, with a more extensive distribution. It is therefore not difficult to separate the corpus mammæ from them. The stroma is loose, and contains numerous fat lobules. The whole is less smooth, firm, and elastic; therefore it tends to be pendulous, and a sulcus is formed where it overhangs its attachment to the thorax. At each succeeding pregnancy there is a new period of activity which is followed by involution.

With the end of the sexual activity a gradual permanent atrophy of the secreting portion of the gland begins. This is produced, according to Stiles, by a fatty degeneration of the epithelium followed by its absorption. The terminal alveoli shrink and disappear as well as the smaller ducts. The atrophy is more or less complete in different individuals and may leave only the ducts. In thin women, the corpus mammæ is represented, after the menopause, by a flattened disc closely related to the skin, and also to the underlying pectoral muscle. The peripheral processes can scarcely be separated from the body, and are reduced to mere irregular threads. In fat women after the menopause the breast remains of a large size, but is composed almost entirely of fat. A few ducts, here and there, form a wide meshwork except in the neighborhood of the nipple, where there is a flattened disc of gland tissue.

Stroma.—Both body and processes are completely covered by a delicate connective tissue. Those parts of this which cover the scattered branched parts of the gland are continuous with the surrounding subcutaneous tissue. It is too delicate to be deserving of a separate name, but has nevertheless been called by some the fibrous capsule of the mammæ. The stroma proper is tough and compact, but soft and yielding. It is white in color and is composed of coarse, wavy fibers. In the nullipara, there is only here and there an isolated fat lobule; consequently the fibers are closely arranged. In the multipara, much more fat is found in the stroma. Toward the periphery more fat lobules are seen, and the stroma of the peripheral processes becomes directly continuous with the connective-tissue framework of the fat lobules.

As stated above, from the apex of the processes on the ventral surface of the gland, the stroma is continued to the corium. These prolongations have received the name *retinacula cutis*, ligaments of Cooper (7, Figs. 1098 and 1099).

Between the ventral processes of the gland, and therefore surrounded by the ligaments of Cooper, are supramammary accumulations of fat (adipose fossæ).

On the dorsal surface of the gland are other fat spaces (retromammary fat) (9, Figs. 1098 and 1099). This is separated from the pectoral fascia by loose connective tissue, and in it one or more large lymph spaces are found, the retromammary or submammary bursæ. The subcutaneous fat and that between the lobules give the smoothness to the surface of the gland, and when it is absorbed, as during lactation or in emaciation, the lobules of the gland stand out much more distinctly.

Under the nipple and areola, the stroma contains no fat. Its fibers are here very loosely arranged, and allow free mobility of the nipple. It is this also which allows the distention of the ducts and sinuses during lactation.

The Skin.—The skin covering the ventral surface of the breast, except at its center, does not differ from that of the adjacent thorax. It is thin, flexible, and very adherent to the subjacent fatty tissue and covered with minute hairs and contains rudimentary sebaceous glands. Following pregnancy the skin is sometimes marked with bluish or whitish striæ similar to those of the abdomen.

Mammary Areola.—Near the center of the skin covering the breast is the areola surmounted by the nipple. The skin of the areola is thinner and more delicate than that surrounding it (Fig. 1105, A). It is pigmented and marked by numerous well-developed sebaceous glands. Its deep surface is devoid of fat, but contains numerous unstriped muscle fibers. The areola measures fifteen to sixty millimeters in diameter. Its color in nulliparæ is a rosy pink, whose shade differs with the complexion of the individual.

In the second month of pregnancy the areola begins to enlarge and darken. This increases as pregnancy advances and serves as one of the signs of gestation. After lactation the color fades, but seldom entirely disappears. In dark brunettes, during pregnancy, the pigmentation becomes very dark, almost black, and following lactation considerable pigment remains. In light blondes, on the other hand, the darkening of the areola is very slight and may subsequently almost entirely disappear. In the fifth or sixth month of pregnancy there is sometimes seen around the areola an irregular slightly pigmented ring, the secondary areola (Fig. 1105, B).

The ventral surface of the areola is roughened by numerous slight elevations. These are caused by well-developed sebaceous glands, *arcolar glands*. At the center of each a minute lanugo hair marks its opening. During pregnancy these glands enlarge markedly, forming hemispherical elevations from two to five millimeters in diameter. They are now known as the tubercles of Montgomery (Fig. 1105). They are particularly numerous and well marked in the secondary areola (Fig. 1105, B). Toward the end of gestation they become very active, their peculiar fatty secretion keeping the areola moist and serving to protect it during suckling.

The sudoriferous glands of the areola are remarkable for their large size and degree of convolution. The areola is not unusually covered with a quantity of well-developed hair, especially in women who have a tendency to the development of hair upon the face.

Besides the above there are from five to fifteen accessory milk glands below the areola. They vary considerably in size, and open on the summit of the nipple. The areolar muscle proper is thickest beneath the nipple and fades toward the circumference of the areola (Fig. 1098). It is composed mostly of circular fibers among which are mixed certain radially disposed bundles. All are attached to the skin, making it therefore a skin muscle analogous to the dartos. After full development has passed the areola begins to form into folds and loses its circular form.

Mammary Papilla.—The nipple is situated a little meso-caudad of the center of the breast on a level with the fourth rib or over the fourth intercostal space and about twelve centimeters from the mid-line (Figs. 1098 and 1099). Developed from the gland area, in the third year it projects from the surface, and soon becomes conical or cylindrical. It attains its full size shortly after puberty. In some cases it is hemispherical, flattened, or discoidal, or with apex larger than base, pedunculated. It is about ten to twelve millimeters long, with a diameter at the base of nine to fifteen millimeters, and points ventrad and slightly laterocephalad. Its tip is rounded and marked by fifteen to twenty minute depressions, milk pores, into which the lactiferous ducts open. These form the cribriform area. In some cases the nipple is retracted into a depression and projects only on response to stimuli. The skin of the nipple (Fig. 1105, 1), thin and pigmented like the areola, is remarkable for the number and size of its papillæ. It possesses neither hair follicles nor sweat glands, but near the base are a number of sebaceous glands.

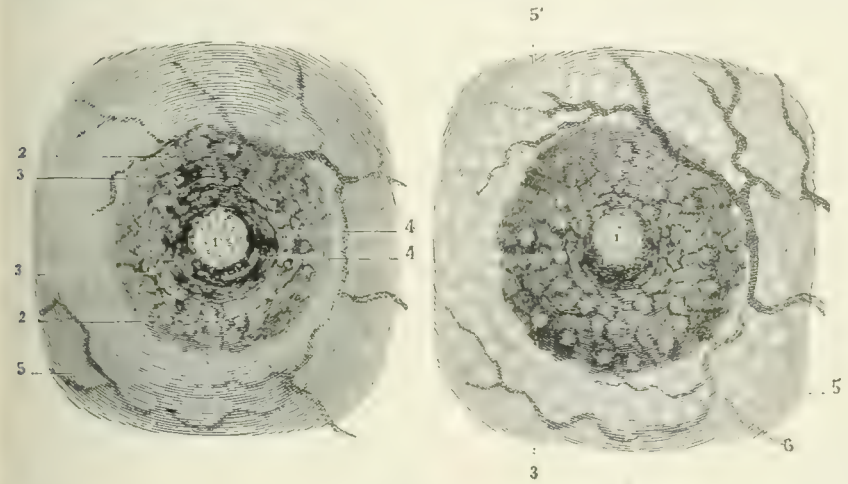

Fig. 1105.—The Nipple and its Areola. A, In a non-pregnant; B, in a pregnant woman. 1, Nipple; 2, areola; 3, tubercle of Montgomery; 4, sulcus at the base of the nipple; 5, skin of breast; 5', secondary areola; 6, venous circle of Haller.

The muscle fibers of the areola are continued up into the nipple, being separated from the skin below only by the sebaceous glands. They form a layer composed almost exclusively of circular fibers. From the inner side of this layer numerous muscle bundles are given off. These cross and recross and form a sort of trellis around the lactiferous ducts. Under the influence of cold, emotion, or touch these contract, causing circular folds in the skin of the areola, and causing the nipple to become firmer and more projecting. Besides causing this erection of the nipple, the rhythmical contraction of the fibers

tends to force the milk from the distended milk ducts and sinuses into the area cribrosa. If the fibers contract spasmodically, they act as a sphincter and retain the milk. Another set of fibers take their origin from the deep connective tissue below the nipple and end upon the under surface of its skin. They pass in variously-sized bundles through the connective tissue which surrounds the milk ducts. Contraction of these fibers causes the nipple to retract.

During pregnancy the nipple becomes larger, more readily erectile, and more sensitive. Suppression and multiplication of the areola and nipple were considered with suppression and multiplication of the gland proper.

Arteries.—The arteries which supply the breast are derived from three sources: from the internal mammary, from the lateral thoracic (long thoracic), and from the intercostal artery. The internal mammary, a branch of the subclavian, is the principal artery of the breast. It gives off two or three branches (rami perforantes), which pierce the chest wall and then pass to the cephalo-mesal edge of the gland, where they break into branches for both of its surfaces. The lateral thoracic, a branch of the axillary, gives two or three branches (external mammary rami) to the external portion of the breast. Besides the above, twigs from the pectoral rami of the acromial thoracic artery pierce the major pectoral and supply the cephalic segment of the breast. Lastly, the intercostal furnishes several small, short branches to the caudal segment and posterior surface. The above vessels, taking a sinuous course, break up into numerous branches which anastomose freely and ramify in the fascia surrounding the gland. From the wide-meshed, irregular network of the ventral surface two sets of branches are given off: one very small to the skin, the other much larger to the gland proper. These latter, situated in the stroma, divide and subdivide on the connective-tissue framework. They finally form a close capillary network which surrounds the acini. The arterioles of the nipple do not form cavernous sinuses, and its erection is due entirely to the muscular tissue. The capillary network in each lobule forms a closed whole and communicates with that of the neighboring lobules only through small arteries and veins.

Veins.—From the arterial capillary plexus around the acini a venous plexus arises. This proceeds toward the ventral surface of the gland and forms beneath the skin a large-meshed plexus. During the period of lactation these vessels are seen through the skin as blue lines. Around the nipple, these subcutaneous veins form a more or less complete ring, the venous circle of Haller (Fig. 1105, B).

The superficial network communicates freely with the superficial veins of the neck above, with those of the abdomen below, and with the thoraco-epigastric vein laterally. These carry the blood into the subclavian, the intercostal, the internal mammary, and the axillary by branches which parallel the arteries.

Lymphatics.—The following description of the lymphatics is in the main that given by Stiles, and differs somewhat from that of other authors. There are five sets of lymphatic vessels: (1) superficial or cutaneous, including those of the nipple, areola, and surrounding skin; (2) subareolar plexus (Sappey); (3) intramammary; (4) those of the circummammary fat; (5) retromammary.

The cutaneous lymphatics are similar to the cutaneous lymph vessels elsewhere. It is to be noted that those of one side of the body communicate with those of the other; thus explaining the occurrence of axillary infection on one side from a tumor of the opposite. Upon the skin of the nipple and areola the network formed by these vessels is very close, being particularly rich upon the nipple. They open mainly into the subareolar group.

The subareolar lymphatics consist of very large vessels, forming a wide-meshed network running horizontally in the loose areolar tissue around the lacteal sinuses. As noted above, the cutaneous vessels open into this plexus, as do also many of the intramammary vessels. It thus serves as a means of communication between the two. From the subareolar plexus of lymphatics Sappey states that there are two and sometimes three large trunks which open into the axillary lymph nodes.

The intermammary lymphatics begin as a plexus of small channels consisting of a single layer of endothelium supported by stroma. Each mesh of the network surrounds one or more of the ultimate lobules of the gland, and receives its lymph from the interacinous spaces. From this layer vessels parallel to the milk ducts proceed to the subareolar plexus into which they empty. Waldeyer describes lymph spaces all around the gland acini.

These periductal as well as the perilobular lymphatics anastomose with others which are closely related to the blood-vessels. The larger blood-vessels are accompanied by two or more lymphatics which occupy their sheaths. The smaller vessels are usually accompanied by only one lymph channel, which is larger than the vessel and more or less completely surrounds it.

The circummammary set receives branches from the skin and the ventral surface and circumference of the breast. It is merely a part of the general lymphatic system of the ventral chest wall. From this set larger lymph vessels proceed between the layers of the deep fascia. They soon pierce the deep layer of this fascia and proceed, as large muscular-walled lymph vessels, to the lymph glands.

The retromammary lymphatics include those of the pectoral fascia. They receive branches from the posterior surface of the gland. Either directly or indirectly some of the lymph from all other sets passes into these lymphatics of the deep fascia which accompany the mammary blood-vessels and thus reach the lymph nodes.

The lymphatics of the medial part of the gland accompany the branches of the internal mammary artery through the chest wall and empty into the sternal lymph nodes situated along this artery. A great many accompany the branches of the axillary artery to empty into the axillary lymph nodes. The retromammary lymphatics of the two breasts communicate.

During the activity of the breast the lymphatics are filled and the lymph nodes are red, solid, and composed almost entirely of lymphoid tissue. During inactivity the lymph vessels are but slightly filled and the nodes appear to take on a fatty change. This is particularly marked in senility.

Nerves.—The nerves of the breast, excluding those derived from the sympathetic, which enter the gland with the arteries, are derived from three sources: first, from the second, third, fourth, fifth, and sixth intercostals; second, from the cervical plexus; third, from branches of the brachial plexus. The intercostals supply the breast by twigs from their anterior and lateral cutaneous branches. The third and fourth cervical nerves of the cervical plexus give off the suprasternal, supraclavicular, and supraacromial. Twigs from the middle of these groups, the supraclavicular, supply the upper part of the breast. From the inner and outer cords of the brachial plexus the medial (internal) and lateral (external) anterior thoracic nerves take origin and pass forward to supply the pectoralis major and minor muscles. Twigs from these nerves pierce these muscles to supply the breast on its deep surface. These nerves receive their fibers from the anterior primary divisions of the fifth, sixth, seventh, and eighth cervical and first thoracic nerves. They

proceed to the gland proper, to the skin, to the muscle fibers below the areola as well as to the blood-vessels. The nerves of the mammary gland resemble those of the pancreas and salivary glands in that they form in the membrana propia a network from which fine fibers extend to come in contact with the glandular epithelium. These fibers form no net or plexus but short granular endings of different configurations and dimensions. Krause and Langer report finding Pacinian corpuscles, never in the connective tissue but in the base of the gland, sparingly also in the nipple. The nerves may end in tactile corpuscles in the papillæ. Brunn in examining two constant nerves in white rats has found that in rats that are neither pregnant or nursing the number of nerve fibers ranges from 307 to 491. In nursing rats the number of fibers varied from 569 to 669 and in pregnant ones from 491 to 655. Thus there is an increase of forty-two per cent. in the number of fibers in the nerves in question between the inactive and active stages. It is not known if there is a like increase in the nerves of the human mammæ.

Stimulation of the mammary nerves causes an erection of the nipple, dilatation of the vessels, and secretion of milk. After section of the cerebrospinal nerves erection of the nipple does not occur, but the secretion of milk is not interfered with. It seems probable that there are special nerves, aside from those of the blood-vessels, governing secretion; but this has not been proved. Emotional disturbances (anger, fear, and so forth) arrest secretion.

From 500 to 1,500 c.c. of milk is daily secreted. To remove this from the gland there is not only the mechanical action of sucking, but also the activity of the gland itself. This latter consists in the contraction of the muscle fibers beneath the areola. By these the nipple is erected and by their rhythmical contraction the milk ducts and sinuses are emptied. The sucking not only stimulates the muscles to act, but also excites the sensory nerves of the nipple, thus causing a reflex stimulation of the gland acini and an increase of the secretion. During activity the vessels of the gland are dilated. The amount of the secretion appears to be influenced by blood pressure. Frequent and rapid emptying of the gland causes a greater flow, possibly through secretion pressure within the cells. The oftener the breasts are emptied the richer the milk becomes in casein. The last milk obtained at any time is always richer in fat, as it comes from the acini.

Human milk is always alkaline. Cow's milk may be alkaline, acid, or neutral. The milk of carnivora is always slightly acid. Various substances, when eaten by the mother, are secreted in the milk. Such are anise, vermouth, garlic, etc.; chloral, rhubarb, opium, iodine, mercury, lead, etc. Some substances, such as atropine, arrest the secretion of milk.

Milk contains large amounts of casein, lactose, and fat, also certain inorganic constituents. Neither the casein nor the lactose occurs in the blood, and fat is found only in small amounts. The inorganic salts in the milk are in different proportions from those found in the blood. Food rich in proteids increases the amount of milk, but the relative amount of fat is increased more than the other constituents. With a pure flesh diet, the milk contains a very large amount of fat. Fat added to the food, if not accompanied by an addition of proteid material, rather diminishes than increases the amount of fat in the milk. It appears, therefore, that the fat in the milk is not obtained from the fat taken with the food, but is the result of the decomposition of the proteid. Increasing the carbohydrates of the food does not increase the amount of sugar in the milk. The greater part of the sugar is therefore also derived from the proteids; so too is the casein. Both the milk sugar and the casein are probably formed by the action of ferments which remain in the cells and do not pass into the milk. It is clear that milk is a chemical product, and that it is due to the activity of the cells in the mammary gland. Concerning the specific chemical source of the constituents, nothing is known with certainty. The relative proportion of the various constituents of the milk varies in the different months after delivery. The cause of this variation is not known, but by it those substances best suited to the child during its different periods of growth seem to be supplied.

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Breast, Diseases of the.—The mammary glands are not only among the distinctive anatomical features of the human species, but they alike serve to designate and to group together into a separate division the higher orders of the animal kingdom thus endowed, that is, the mammalian class of vertebrates.

In the human being the breasts constitute two hemispherical bodies resting on the anterior aspect of the thorax, on either side of the sternum, and are present in both sexes, although in the female they secrete the milk for the sustenance of the infant. The female breast, moreover, becomes large and prominent and is subject to a series of characteristic evolutionary changes; while the male breast retains its embryonic type until near middle life, when it undergoes retrogression and atrophy.

Development.—It can be safely assumed that the mammary glands originate in a group of finely specialized sudoriparous glands. There is no difference of opinion among embryologists as to their development from the glands of the epiderm, but the point of contention is, whether these glands are of a sebaceous or sudoriparous type. But the evidence is so strongly in favor of the latter, that it seems now to be the generally accepted view that the highly organized milk gland is the evolved product of the sweat gland.

In very early embryonic life in the pig and other animals, Schultze found, extending from the foreleg to the inguinal fold on either side, a light streak, along which the mammary glands later developed, to which was applied the name of mammary streak. This was found in the human embryo by Hirschland and Strahl, and results from the cells of the ectoderm penetrating deeper and becoming more cubical. In this streak or line the epithelium multiplies more rapidly at points corresponding to the future glands, thus forming the mammary hillocks (Bonnet). About the end of the second month of fetal life, these small tubercle-like thickenings of the epidermal layer gradually increase. This change, as Minot states, is very slight at first, and begins where the epidermis is composed of an inner and an outer layer, but is exclusively confined to the inner or germinal layer. Somewhat later this mass of cells assumes a flask-like shape—a rounded form with a slight projection, the intended nipple—which pushes downward as an ingrowth into the derma. This ingrowth increases in size, its central cells gradually harden or cornify and drop out, leaving the ingrowth excavated. This excavation or hollow progresses very slowly, and occasionally is not completed until just after birth or even later. Shortly following the commencement of this hollowing out, the ingrowth sends out buds that resemble in appearance and development genuine sweat glands, which view both Minot and Gegenhauer maintain. Coincident with this excavating process a depression is formed at the point corresponding to the future nipple, and which is later filled out by the formation of the nipple. This depression sometimes remains uneffaced to a greater or lesser degree, resulting in a deformed or depressed nipple. The mammary gland is evolved by a budding from the deeper portions of the original mass of epiderm. The branching of the buds which form the glandular tissue commences about the seventh month; the first appearance of the lumen of the glands is at the lower ends, which become increased in size and clubbed, and extends toward the mouth of the gland. At an early date can be seen, surrounding and supporting these glandular elements, a stroma of fibrillated connective tissue, within which the development and growth of the glands proceeds.

At birth the gland is composed of a number of radiating ducts with clubbed extremities but without definitely formed acini. The duct epithelium is sometimes in an actively proliferating state, producing dilatation of the ducts and swelling and tenderness of the glands, a supposed inflammatory condition—mastitis neonatorum—which occurs from the fourth to the tenth day. At the same time a milky secretion may exude from the nipple, the so-called "witches milk." It is possible for infection to enter through the nipple and cause this condition, but everything indicates that it is rather a normal glandular developmental activity. Therefore in the ten days succeeding birth changes take place producing some acinous tissue, but only the main ducts are hollowed out. From this time but little change occurs, the intralobular ducts and beginning of the acini continue solid, and this state remains unaltered up to the period of puberty. In the male there is no further development, and the breast structure retains its rudimentary character.

After this, scarcely any change in the appearance or anatomy of the breast takes place until the period of puberty. At this age the development of the acini actively begins, together with the formation of ducts, and this is often accompanied by an enlargement and decided tenderness of the breast. This may also occur in the male.

At each menstrual epoch a mild engorgement of the breast recurs, attended by a pricking sensation, and it is probable that this condition indicates further development at these stages. In a short while after the onset of puberty the mammary glands undergo rapid developmental changes, although they consist principally of stroma and excretory ducts, with only proportionately a small amount of gland tissue. The connective tissue surrounding the gland tubes also takes on active change, assuming an uncommon hyaline form, richly nucleated, which presents a striking contrast to the interstitial connective tissue that fills the spaces between the lobes of the gland. This semitransparent periductal substance exists only in the mammary gland, and is the framework giving the shape and density to the young breast. It has been carefully studied by Warren, and he particularly emphasizes the importance of this tissue both as to the subsequent vascular formation at the time of gestation, and as being the starting-point of certain types of neoplasms.

With the occurrence of pregnancy and lactation the vascularity of the tissues becomes quite increased, epithelial proliferation is most active, and there is an excessive multiplication of acini. After lactation ceases the acini shrink, but there is no contraction of the connective tissue, and, consequently, the breasts do not regain their former firmness but remain flabby or pendulous.

When the breasts have passed the period of functional activity and the stage of decline is reached, the glandular tissue atrophies, the epithelium disappears, with final collapse of the acini. The ducts alone remain as lengthened tubes at the ends of which can be seen remnants of the atrophic acini of the gland; the glandular structures are replaced by fatty tissue. When the final stage in the life history of the gland is completed, there is left scarcely a trace of gland tissue, the breast structure being composed alone of elongated tubes along with connective and adipose tissues. It is at this period of mammary degeneration that the ducts often undergo dilatation of a cystic nature, and may not infrequently assume pathological features.

Anatomy and Surgical Relations.—The mammary body is a glandular structure of the compound racemose type. There are normally a pair of breasts, which are situated beneath a covering of fat and skin, on the anterior aspect of the thoracic wall, one on either side of the sternum. Somewhat mesocaudad of the center of the breast and pointing slightly in an upward and outward direction, projects the conical-shaped nipple surrounded by the areola. Haidenhain, Oelsner, and Stiles have shown that the common estimate of the area occupied by the breast is largely based upon the external dimensions and conformation of the organ, and does not agree with its actual size and contour. Stiles gives the measurements as follows: Extending in a vertical line from the lower border of the second rib to the sixth costocartilage, from which point it begins to pass rapidly upward toward the sternum, and horizontally from just within the outer border of the sternum opposite the fourth rib or interspace to the midaxillary line at the level of the fifth rib or interspace. The level of the breast varies with the height of the individual, being lower in tall and higher in short and broad-chested women. It is also considerably displaced upward and outward when the arm is elevated and drawn away from the body, as in the position for operation.

The gland rests posteriorly for the greater part upon the fascia of the great pectoral muscle and slightly on that of the pectoralis minor muscle, on the fascia covering the serratus magnus muscle, and on the external abdominal oblique muscle. The intimate relationship between the gland and the pectoral fasciæ is of special importance in connection with malignant disease of the breast. Along its inner and inferior quadrant the gland is rather distinctly outlined from the fat, and is also more intimately attached to the deeper fascia by bundles of fibrous tissue, the so-called mammary ligaments. Carcinoma located here usually forms early and deep adhesions. The gland is of an irregular circular or tricuspid shape due to the several projecting processes of the parenchyma. Of these prolongations there are three principal ones, the longer one known as the "axillary tail," projects toward the upper part of the axilla; another, smaller one, reaches toward the lower part of the axilla; and a third extends in the direction of the sternum. In addition to these prolongations other small outward extensions of parenchyma exist between the gland and the skin, along the ligaments of Cooper, and also downward to the major pectoral muscle, and, again, even processes project into the surrounding fat. There are also a number of adjacent and separate masses of gland tissue frequently found, the paramammary glands. The parenchyma is furrowed at its lower border, which depression is especially marked in stout women and in multiparæ.

The under or dorsal surface of the breast is slightly concave and largely composed of stroma-holding radiations from the parenchyma. The stroma is continuous with the loose pectoral fascia, and joins with it in sending out numbers of trabeculæ in between the fibers of the subjacent muscle. This fascia is delicate and loose, but in thin subjects it is often difficult to strip from the muscle, and in some persons it is so tightly adherent that movements of the arm may produce marked displacement of the breast. Spaces, or serous bursæ—submammary bursæ—were found by Chassaignac in this loose areolar tissue.

The outer surface of the breast is smooth and covered with integument of the same texture as the surrounding surface of the body, except near the center where it is raised and pigmented, forming the areola, with the projecting nipple. In plump, healthy, unmarried women it is conical in shape, but this differs with the degree of stoutness or thinness of the individual, and in virgins and in those who have lactated. The consistency also varies in the nulliparous and multiparous breast, being firm and elastic in the former, and softer and flabby or even pendulous in the latter class.

In size the breasts are often unequal, sometimes one, usually the left, being much larger than its companion, probably an hypertrophy due to more constant nursing of the child on the enlarged side. Race also influences the size, the African races having very large and pendulous mammæ. But the volume does not indicate the size of the gland structure, since the largest breast may possess but little secreting tissue.

Structure of the Mammary Gland.—In structure the mamma consists of a parenchyma and a stroma, similar to other glandular structures. It should be remembered, however, that the anatomical structure of the mammary body is not permanent, but changes with the varying stages of its life history. In the mature female breast the parenchyma is made up of a central compact triangular mass, the body of the mamma, with its apex at the nipple, and peripheral processes. It is divided into lobes, fifteen to twenty in number and arranged radially, which are subdivided into lobules, and these again into acini. All of the lobules empty by a duct into larger and larger ducts, and finally into the large lobular or lactiferous duct, which in turn empties into a milk pore, a little depression on the surface of the nipple. Every lobe represents a separate and distinct gland. The spaces separating them are filled with fatty tissue. Each lobule with its acini is embedded in a loose myxomatous intralobular connective tissue, and is then enclosed, including nerves and vessels, by the tough interlobular stroma. The acini have an epithelial lining of granular cells resting on a delicate membrana propria, and the ducts are also lined with one layer of columnar epithelium. The large ducts correspond to the fifteen or twenty lobes and converge toward the nipple on which they terminate in the milk pores; but before thus ending they dilate into ampullæ beneath the base of the nipple.

The stroma is a white, tough, though soft and elastic, structure. From its anterior surface numerous fibrous prolongations or bands extend into the dermis, forming the *ligamenta suspensoria* of Cooper. These so-called ligaments are of particular diagnostic value in early malignant disease of the breast. They are often connected with paramammary glands and lymphatic vessels, and it is to the cicatricial contraction of these bands that the dimpling or depression of the integument in cancer is due.

Structure of the Nipple and Areola.—The nipple is placed a little above and mesad of the center of the breast, about on a level with the fourth rib. It is a cone-shaped body and formed by an elevation of rugous, reddish-brown skin. At its summit are from fifteen to twenty depressions, or milk pores, into which open a corresponding number of galactophorous ducts. The nipple is supplied with circular muscle fibers which, under the stimulus of emotion, touch, or cold, contract and produce erection of this body, and still others that cause its retraction. There are no cavernous sinuses in the nipple, and its erection is controlled entirely by muscular action. Surrounding the nipple is the areola, a circle of dark-hued, pigmented, delicate skin, and marked by a number of sebaceous follicles, known as the tubercles of Montgomery. The assertion by Rein that these are accessory milk glands is now believed to be erroneous. The areola contains numerous unstriped muscle fibers, but its under surface is wholly free from fat. Its color varies with the complexion of the owner, and it enlarges and becomes more deeply pigmented with the accession of pregnancy.

Lymphatic Distribution.—In view of the frequency of new growths of the breast, the lymphatic vessels of the mammary gland and their intimate association

with neighboring structures and organs, assume an importance that cannot be overestimated. Whereas in the male breast the lymphatics scarcely differ in development from those of the surrounding tissues, in the female the mamma is more richly supplied with lymph vessels than any other gland of the body.

In the present discussion of the mammary lymph vessels I have, to some extent, followed the description given by Stiles, from whose paper, and from the article of Kerr, I have rather liberally drawn.

Five divisions of lymph vessels may be recognized: First, the cutaneous division; second, the subareolar plexus of Sappey; third, the intramammary; fourth, those of the fat surrounding the breast; and fifth, the retromammary.

(1) The distribution of the *cutaneous lymphatics*, which include those of the breast skin, areola, and nipple, does not differ from that of the superficial lymph vessels of the adjacent skin. They are composed of two networks or plexuses, and each sends efferent trunks leading to the axilla. These trunks may occasionally turn back to the skin, which explains, according to Oelsner, some cases of skin metastases. There is free intercommunication between the skin lymphatics of the two sides of the body, which accounts for those cases of axillary infection of one side being associated with tumor in the breast of the opposite side. The lymphatic network of the skin of the areola and nipple is very fine and close meshed, especially on the nipple, and empties, for the most part, into the subareolar plexus.

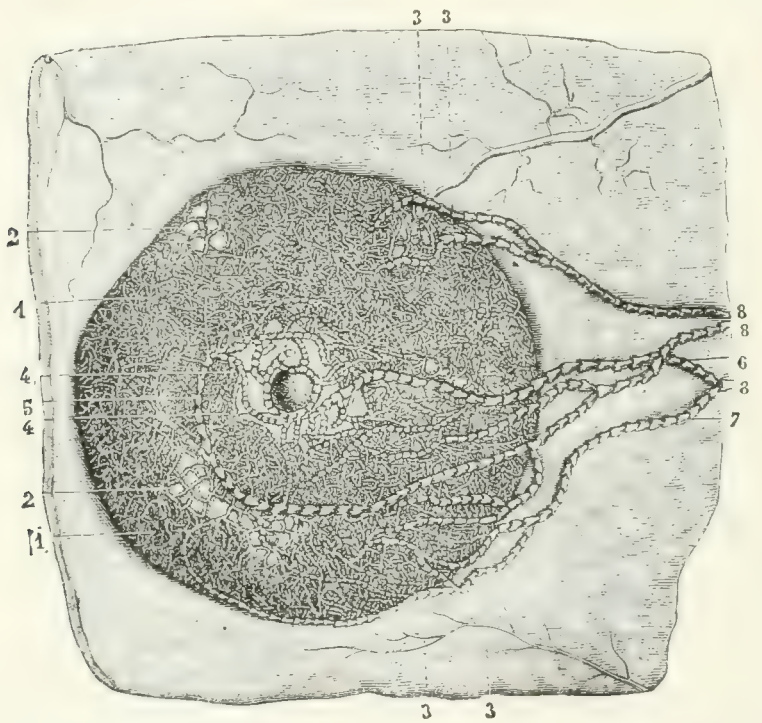

Fig. 1106.—Lymphatics of the Female Breast. 1, 1, Lymphatic network of the anterior surface of the mammary gland; 2, 2, lobules of the mammary gland, the peripheral lymphatic network of which has not been injected, in order to render more prominent the circumlobular network which surrounds the lobules; 3, 3, trunks which arise from the upper and lower portions of the mammary gland; 4, 4, lymphatic plexus under the areola; 5, lymphatic vessel which arises from the internal part of this plexus and which takes a semicircular course to reach the axilla; 6, another vessel arising from the outward part of the same plexus and running directly outward; 7, lymphatic vessel arising from the lower part of the gland and uniting with the preceding to form one of the two trunks into which all the other vessels empty; 8, 8, vessels arising from the internal part of the subareolar plexus and from the upper portion of the breast converging to form the second of the two trunks which empty into the axillary lymph nodes. (Sappey.)

(2) The group of *subareolar lymphatics* consists of a network of large vessels, occupying a horizontal position in the loose areolar tissue around the lacteal sinuses. Sappey has demonstrated that two and often three large trunks from the subareolar lymphatic plexus empty into the lymph glands of the axilla, thereby putting the nipple and areola in direct communication with that space.

(3) *The intramammary lymphatics* arise as a plexus of minute channels, made up of a single endothelial layer sustained by stroma, and each one of the meshes of this surrounds one or more of the terminal lobules of the gland, and receives the lymph from the interacinous spaces. From this layer vessels make their way, in a direction parallel to the lacteal ducts, to the subareolar plexus into which they empty. These periductal lymphatics together with the perilobular lymphatics, inosculate with other vessels in close relation with the blood-vessels. The larger blood-vessels have within their sheaths two or more accompanying lymph vessels. The smaller blood-vessels have only one such lymph channel associated with them, but this is larger than the vessel and surrounds it to a great extent.

(4) The *circummammary* division is simply a part of the general lymphatic system of the anterior chest wall, and receives branches from the skin of the ventral surface and the circumference of the breast. From this division larger vessels branch and extend out between the layers of the deep fascia, pierce the deep layer, and pass on as large muscular-walled lymph trunks to the lymph nodes.

(5) The *retromammary* lymph vessels embrace those of the pectoral fascia, and receive branches from the under surface of the gland. A portion of the lymph gathered from all the other lymphatic divisions, is conveyed, either directly or indirectly, into these lymphatics of the deep fascia which accompany the mammary blood-vessels and by this route reach the lymph glands. Free communication exists between the retromammary lymphatics of the two breasts.

The lymphatic vessels of the inner segment of the breast, in company with the branches of the internal mammary artery, perforate the chest wall and empty into the anterior mediastinal nodes situated along that artery in the loose substernal areolar tissue. A large number follow the branches of the axillary artery to empty into the axillary lymph glands. An important lymph vessel, and one that is rather regular in this position, comes out from the base of the gland, pierces the great pectoral muscle and runs upward between it and the lesser pectoral muscle along the thoracic wall to a point just below the attachment of the pectoralis major, where it perforates the second intercostal space to enter the anterior mediastinum. The deep lymphatics of the gland inosculate freely with those from the deep pectoral fascia. Many authorities (Seidel, Schweigger, Ludwig, Rotter, and others) claim that the direction of the lymph stream is from the pectoralis major muscle (especially the superficial portion) toward the fascia and not in the opposite course. The lymph vessels coming from the clavicular portion

of the muscle flow into the retropectoral glands; those of the upper sternal portion empty into the supraclavicular nodes. Chains of lymph nodes accompany the large blood-vessels throughout their length, in close relation with the vein; and they extend from the bottom to the top of the axilla, forming three principal groups, namely, the pectoral, the axillary, and the subscapular groups. The glands of the pectoral group are placed beneath the outer edge of the great pectoral muscle, and are the nodes which are usually the earliest to become infected in mammary carcinoma. Next to these is the axillary cluster located in the loose adipose tissue of the axilla, forming a network covering the anterior aspect of the axillary vein. This group also receives vessels coming from the subscapular group of lymph nodes, which latter do not directly connect with the breast but receive lymph vessels principally from the thoracic wall and postcervical regions. This last group of glands is frequently infected from below on account of their extensive anastomotic association. The lymphatics coming from the axillary group accompany the axillary vein (being principally placed on the inner surface), and then pass on by means of one or several large ducts to the right lymphatic duct. These lymphatic vessels inosculate with the subclavian and deep nodes of the posterior cervical triangle.

Blood Supply.—The arterial supply of the breast is principally derived from three sources, namely, (1) the internal mammary, (2) the intercostal, and (3), the long or lateral thoracic. The internal mammary is the principal artery of the breast, and sends off the anterior intercostals which perforate the intercostal muscles, which they supply, and then pass to the upper and inner margin of the gland where they divide into branches for both the anterior and posterior surfaces. The intercostal supplies several small and short branches to the posterior surface of the gland and its caudal segment. The long thoracic comes from the axillary, anastomoses with the above vessels, and furnishes several branches to the external portion of the breast. In addition to these vessels, small branches from the pectoral branches of the acromial thoracic artery perforate the pectoralis major muscle and pass to the upper portion of the gland.

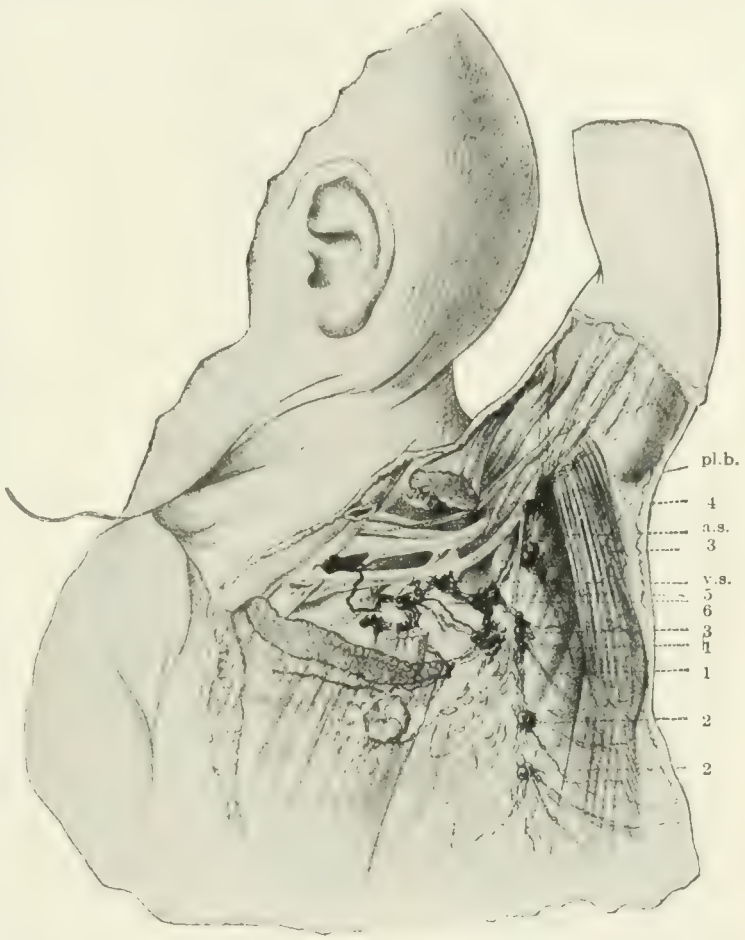

Fig. 1107.—Lymphatics of the Axilla. 1, 1, Anterior thoracic lymph nodes; 2, 2, inferior lymph nodes; 3, 3, posterior or subscapular thoracic nodes; 4, superior brachial thoracic nodes; 5, intermediate thoracic nodes; 6, subpectoral and subclavicular thoracic nodes; *pl.b.*, brachial plexus; *a.s.*, subclavian artery; *v.s.*, subclavian vein. (Oelsner, Archiv. f. klin. Chirurgie, lxiv., 1901.)

The venous return from the mammary gland arises in the arteriovenous capillary plexus around the acini, and passes toward the outer surface of the mamma and into the subcutaneous tissues. Around the base of the nipple the subcutaneous veins anastomose to form almost a complete venous circle, the "circulus venosus" of Haller, from which large veins carry the blood to the periphery of the breast. From this region the blood is transmitted to the superficial cervical veins, below to those of the abdomen, and laterally to the thoraco-epigastric vein, through which it is conveyed to the *venæ comites* of the arterial supply.

Nerve Supply.—The nerve supply also comes from three principal sources: (1) From the second to the sixth intercostal nerves; (2) from the anterior and posterior thoracic nerves; and (3) from the cervical plexus. The intercostal nerves send filaments to the breast from their anterior and lateral cutaneous branches. The internal and external anterior thoracic and long thoracic (external respiratory nerve of Bell) nerves arise from the brachial plexus and fifth and sixth cervical, pass forward to supply the major and minor pectoral muscles, together with penetrating twigs to the posterior surface of the gland, and proceed to the gland proper, to the skin, and the subareolar muscle fibers. The third and fourth cervical nerves of the cervical plexus, through the suprasternal, supraclavicular, and supraacromial, form the third source of nerve supply, especially to the upper part of the breast.

Some of the nerves may terminate in Pacinian corpuscles in the areola and in the papillæ of the nipple. Stimulation of the nerves supplying the nipple produces its erection, also dilatation of the vessels, and milk secretion.

The anastomosis of the intercostohumeral, a cutaneous branch of the second intercostal, with the lesser internal cutaneous branch (nerve of Wrisberg) explains the severe pain in the arm and side of the chest in certain diseases of the breast.

Congenital Anomalies of the Breast and the Nipple.—The mammary gland and its nipple are subject to various congenital abnormalities and structural defects, the result of arrest in development or to a reversion to original types, and may occur

at any period of the evolution of the breast. These malformations are more often associated with some other congenital deficiency, particularly of the sexual organs, absence of the pectoral muscles, deformity of the chest wall, and in acephalism. They are found in both sexes, and involvement of both breasts in the same individual has been observed.

Absence of the Breast (Amastia; Amazia).—When developmental disturbance takes place early in embryonic life, before the third month, the formation of the mammary gland is entirely arrested. This abnormality is very rare, and is frequently accompanied by other congenital defects usually not compatible with extrauterine life. The ovary on the side corresponding with the defect is occasionally wanting. The right breast is more often absent than the left.

Total absence of both mammæ is one of the rarest anomalies, and Roger Williams states that, excluding acephalic monsters, he was able to find only four such instances in the literature. A case of bilateral amazia is reported by Voglie, in which the woman became pregnant. It is probable that absence of one breast and a rudimentary state of the other is the most frequent form of this anomalous condition found in the adult.

Micromastia (Micromazia).—Arrest of development at a later stage of uterine life, or if the disturbance be incomplete, a small, imperfectly formed or rudimentary gland results—micromastia—which is functionless. This may involve one or both breasts, and may be associated with genital deficiencies. Williams states that the mammary glands are imperfectly developed in the Bavarian women, due to hereditary influences resulting from the custom of not suckling their children, which has been prevalent among them for long years of time.

Supernumerary Breasts (Polymastia; Polymazia).—Plural mammæ is a rather common anomaly, more so than was at one time supposed, and the literature abounds in records of such examples. The statistics of Bruce show that in 4,000 examinations the deformity was present in 1.54 per cent.; and in 315 individuals of both sexes, indiscriminately taken, supernumerary glands existed in 7.6 per cent.; in 207 males, 9.1 per cent.; in 104 females, 4.8 per cent.; and that men, in the proportion of 4 to 1, are more frequently affected than women. This latter conclusion is the reverse of that arrived at by Godfrain and others, who have determined the greater proportion to be in favor of the female sex.

The theory of the atavistic origin of accessory mammary glands offers the most rational explanation of their existence, and investigations in embryology and comparative anatomy seem to substantiate this position. Roger Williams, Orth, and other investigators maintain that the milk gland is the homologue of but a single sebaceous gland,* and that it is impossible for an organ so finely specialized, which required vast æons of time to reach its present perfected state, to be suddenly evolved as "spasts" from ordinary sebaceous and cutaneous processes, as set forth by Ahlfeld and others. This theory is supported by the belief that our early progenitors were supplied with seven pairs of mammæ situated along the ventral aspect of the trunk, three above and three below the present natural pair. Moreover, it is a suggestive fact that the accessory glands are more often seated along the course of the so-called "milk line"—a line on the ventral surface extending from the axilla to the groin, and corresponding with the mammary ridge along which the mammæ are normally situated in polymastic animals.

Supernumerary breasts are frequently in pairs, and when unilateral they are oftener found on the left side than on the right side, and above the level of the umbilicus than below it. The ordinary site is somewhat below and internal to the normal glands, in which position three-fourths of all the cases are so placed. The next most prevalent position is above the natural ones and toward the axilla. When below the normal breasts they are apt to be more fully developed and provided with better formed nipples. Leichtenstern's table of 105 cases shows the relative position of accessory breasts to be, the anterior side of the thorax ninety-six cases, and axilla five cases (four cases were wandering). It is probable that many of the axillary accessory mammæ are prolongations or sequestrations from the normal breast, and may be mistaken for lymph nodes, sebaceous cysts, and

Fig. 1108.—Supernumerary Nipples and Small Mammary Glands in the Axillæ. (McGillicuddy, Medical Record, October 10, 1891.)

fatty tumors. Occasionally they are met with in various localities outside of the "milk line," as the axilla, the anterior mid-line, abdomen, back, on the shoulder, hip, thigh, labium, the lip, and the ear; and in a few instances they have been noted occupying the inner wall of dermoid cysts of the ovary. Leichtenstern and Bruce in a collection of 166 cases of multimammæ found only four (2.41 per cent.) aberrantly disposed. When occupying such aberrant sites they are designated "mammæ erraticæ," and are supposed to be caused by a reversion to an ancestral type much more remote than the other more usual forms. In polymastia the normal pectoral breasts are always naturally situated and well developed.

The number of accessory breasts may vary from one to as many as ten. Hirst mentions the case of a negress with nine mammæ and nine nipples. Their characters also largely vary. Some of them include only a vestige of glandular structure and are functionless, while others may be large, well formed, and functionate actively. Numerous examples of such are on record, and among these, and of special note, is the case of a woman with five mammæ, all of which yielded milk. Roberts reports the case of a woman who possessed a supernumerary mamma on the outer aspect of the left thigh from which she nursed her own child for the period of two years, together with four foster children for six years. A case reported

* The weight of opinion is in favor of the sudoriparous rather than the sebaceous glands, as the source from which the mammary gland is evolved. See the section on Development, above.

by Hardman of polymazia in a negress, thirty-nine years old, is interesting in that the accessory mamma did not develop until the fifth gestation, there being no evidence of its existence prior to that time.

Sometimes there is no glandular tissue demonstrable, the nipple alone, with or without an areola, being present. There may be entire absence of the nipple and areola—the ducts of the gland opening on a flat surface by one or several openings; or there may be no communication whatsoever with the surface.

The condition is probably common to all races, but would seem to be more so in the negro race (Tiffany); and that heredity often plays an important rôle is also apparent, Leichtenstern showing that in 7.6 per cent. of his series there was such a history in near relatives. It is not usually accompanied by other congenital deformities. These accessory structures follow the same evolutionary changes characteristic of the normal gland, as to both lactation and the menopause. Several observers have referred to the interesting fact that the occurrence of tumor-changes in true accessory mammæ is practically unknown, only one or two questionable cases having been published. Kayser, however, in a report comprising four cases, mentions that in one of them primary carcinoma developed in one of the breasts.

Fig. 1109.—Supernumerary Mamma of the Thigh. (McGillicuddy, Medical Record, October 10, 1891.)

The diagnosis of accessory breasts is usually obvious, but often they may be so small that their nature can be determined only by excision and microscopic examination. When the nipple is wanting the glandular mass may be readily mistaken for a fatty tumor which it closely simulates, for axillary lymph nodes, or for a sebaceous cyst. Supernumerary nipples without associate breasts may resemble pigmented moles and nævi.

No treatment is needed except for cosmetic purposes, or in the event of intercurrent conditions demanding surgical intervention, when excision of the structure or structures should be performed.

Absence of the Nipple (*Athelia*).—Absence of the nipple exists much more commonly than absence of the mammary gland itself, and results when developmental arrest takes place early and is complete. Williams states, however, that there is actually no deficiency in the mammillary structure, but simply a failure of the embryonic gland area to project or become elevated.

Deficiency of the nipple is often attended by absence of or an imperfectly formed areola, but the areola is seldom absent if the nipple is normally formed. Varying degrees of imperfections exist from complete absence to the almost perfect or normal nipple. The lesser defects are comparatively frequent, as seen in the small or flattened nipple and the depressed or inverted organ, and are the frequent cause of inflammations of the gland during lactation.

Supernumerary Nipples (*Polythelia*).—Multiple nipples are relatively of frequent occurrence, especially in the male subject in whom as compared with the female it is stated to occur in the proportion of two to one. The number of nipples may vary from one to even ten or more: Neugebauer reports a

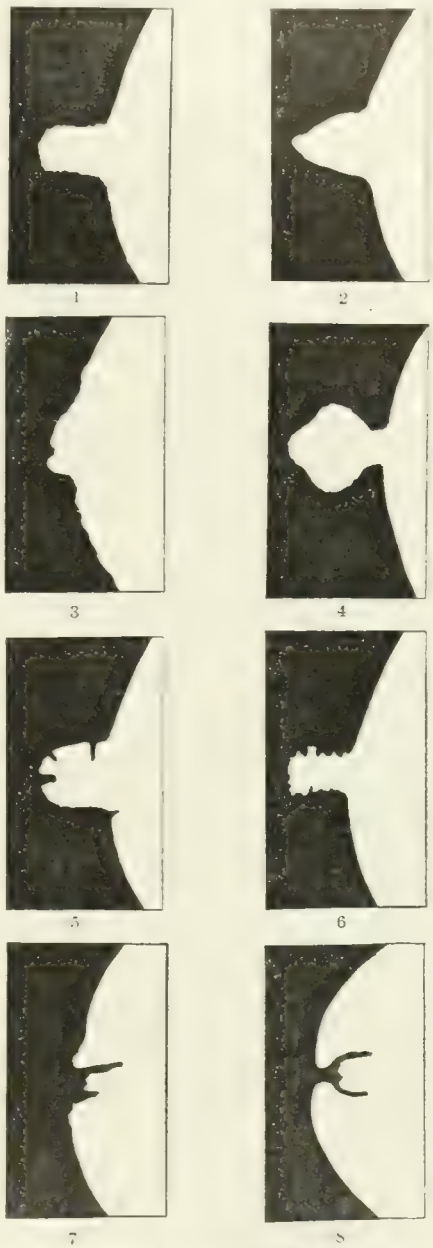

Fig. 1110.—Illustrating Various Forms of Faulty Development of the Nipple. 1, Normal nipple; 2, cone-shaped nipple; 3, stunted nipple; 4, mushroom nipple; 5, fissued nipple; 6, mulberry nipple; 7, retroverted nipple; 8, engulfed nipple. (Reder, Am. Journal of Obstetrics, December, 1910.)

case of polymastia with ten nipples. The case of a mulatto male is mentioned by Alexander, in whom there were six nipples arranged in two vertical rows, with a space of four inches vertically between the nipples; and this patient asserted that his mother was similarly deformed, four of her nipples yielding milk,

and also that one sister and several brothers each possessed four supernumerary mammæ. Homaüs records a case having five nipples on one breast.

This malformation may be simply a bifid condition or cleft nipple; or, when the defects arise late in the process of development, there may be two nipples superimposed on one areola—*intraareolar polythelia;* or several nipples and areolæ on one breast—*intramammary polythelia.* Again, the nipple may be located on parts of the body more or less distant from the pectoral region.

Excision should be practised as conditions may demand.

Hypertrophies of the Breast.—*Congenital Hypertrophy.*—At birth the structure and general characters of the mammary glands are apparently identical in the two sexes, at which stage of growth they are composed of ducts and acini, some well developed and others imperfectly so, enclosed in a loose fatty connective tissue. But commencing immediately after birth the breasts assume rapid developmental changes and cell proliferation in the ducts, which sometimes exceeds the normal limits and produces an overgrowth of the gland, accompanied by the secretion of a milk-like fluid similar to colostrum. This condition is known as *congenital* or *infantile hypertrophy,* and is not infrequently found in connection with precocious development of the sexual organs in young infants. It has been suggested that this condition is similar to the early sexual development occurring in female children in tropical countries.

Fig. 1111.—Precocious Development of the Breast in a Child Four Years and Nine Months Old. Menstruation began at the age of fifteen months. (Mudd, Am. Practice of Surgery.)

Physiological Hypertrophy.—This type of hypertrophy represents the natural enlargement of the mammary gland associated with certain changes incident to pubescence. Until the period of puberty is attained there is no perceptible difference in the structure of the male and the female milk-gland, but at this time further development in the male ceases, whereas in the female breast renewed evolutionary changes begin and progress until the menstrual function is fully established. After this period the mammary changes again remain in abeyance until stimulated to renewed activity by gestation, at which time marked hypertrophy takes place and steadily goes on to the time of lactation, when the gland arrives at its highest state of organization.

According to Dennis there is a true physiological mammary hypertrophy of gigantic proportions; but, if it ever exists, it is extremely rare, and histological examinations have not substantiated this view.

Diffuse Idiopathic Hypertrophy.—This form is pathological, and is practically always bilateral in the female breast. The few cases of unilateral hypertrophy, other than in the male, that are found in the literature are of doubtful pathology, and probably should be classed with the fibroadenomata. Of the seventy cases collected by Albert, six were stated to be unilateral—three on the right and three on the left side.

Fig. 1112.—Case of Diffuse Fibroma of the Breast with a tendency to intracanalicular growth. (C. B. Porter, Trans. Am. Surgical Association, 1891.)

Two varieties of diffuse idiopathic hypertrophy are recognized, (1) the virginal, which is the most frequent, and (2) the gestational form, which is less commonly met with.

(1) *Virginal Hypertrophy.*—This lesion is of the younger female breast, is relatively rare, and is characterized by a symmetrical enlargement of both mammæ. The enlargement begins, as a rule, near the period of puberty or even later, although in some instances the affection would seem to have no re-

lationship with either puberty or pregnancy. In Albert's collection of fifty-two cases, fifty-eight per cent. were of this variety, and developed between the ages of eleven and sixteen years—forty per cent. of the fifty-eight per cent. occurring during the fourteenth and fifteenth years.

In the greater number of cases the affection is of slow progress—a gradual enlargement often covering several years—but occasionally the onset is sudden and the case runs an acute course. Sometimes acute exacerbations occur at intervals; these are more often

Fig. 1113.—Bilateral Diffuse Virginal Hypertrophy of the Breasts in an Unmarried White Girl of Sixteen Years. The left breast weighed seven and three-fourths pounds, both breasts eighteen and one-fourth pounds. (Dr. George Ben Johnston, Transaction of the Southern Surgical and Gynecological Association, 1903.)

near the menstrual epoch. In the few recorded cases where pregnancy supervened, that condition does not appear to have exercised any material influence over the course of the affection, but it has been observed that under these circumstances the milk secretion was either defective or the glands were entirely functionless. The duration is indefinite

(2) *Gestational Hypertrophy.*—Diffuse hypertrophy of the breast occurring during gestation is less common than the virginal type. Of the eighteen cases in Albert's collection, he states that fourteen were bilateral and four unilateral. In this variety the onset is invariably acute, the growth and course is very rapid; it attains its height by the end of gestation, and, as a rule, completely subsides with the completion of pregnancy. It more often than otherwise recurs with each subsequent gestation. The hypertrophy is not always confined to the first pregnancy, but may appear during subsequent pregnancies, and even has been encountered as late as the eighth gestation. Usually gestation is normal.

Etiology.—The etiology is obscure. The pubescent state, pregnancy, and disturbance of menstruation are the only accepted etiological factors; for neither heredity, racial conditions, traumatism, excessive sexual indulgence, nor climatic influences seem to have any relationship to the disease. J. Collins Warren believes that the histological findings sufficiently explain the course of the affection without looking to doubtful theories.

The experiments of Lane-Clayton and Starling on the production of increase in size of the milk glands in virgin rabbits, by the injection of extracts prepared from the body of the rabbit fetus, is interesting. Their conclusions were that the mammary enlargement during gestation is effected by means of a hormone produced in the fetus. These results would suggest, as Albert remarks, the action of a similar hormone in the human fetus as the cause of the gestational type of diffuse idiopathic hypertrophy, and the probability of which is increased by the fact that the disease usually declines after parturition.

The cause of the natural increase in size of the mammæ at the period of puberty is equally if not more obscure. Albert believes that the theory of a hormone in the ovaries can be applied here, and is quite probably the material factor in the production of this, together with the virginal, variety of mammary hypertrophy.

Hypertrophy of the mammæ is occasionally associated with gigantism of an upper extremity.

Pathology.—Inspection of a section of the hypertrophic breast shows a glistening white, smooth surface, not materially vascular, and without evidences of cyst-formation. Sections of dilated ducts and parenchymatous tissue are seen scattered about. The tissues are firm to the touch; and the subcutaneous fat is atrophic.

Microscopically the process is shown to consist principally of a growth of young connective tissue, together with the existence of cell proliferation and hypertrophy of the parenchyma. Warren describes the changes as a peritubular and acinous growth of fibrous tissue containing many nuclei, and it is the large quantity of this growth and its diffusion throughout the gland which distinguishes it from the class of fibromata. It is evident, therefore, that the condition is an exaggeration of the physiological tissue growth at the stage of puberty.

The degenerations of both sarcoma and carcinoma are known to occur in diffuse mammary hypertrophy, but this is uncommon, and until within recent years such changes had not been observed. Bloodgood, writing in 1908, states that during the last two years he had seen carcinoma in conjunction with diffuse hypertrophy in two women, both over twenty-five years of age.

Symptoms and General Course.—The affection does not always start with the changes of puberty, and may not appear until a much later period. It frequently commences as a localized enlargement in a portion of one gland, which goes on to a general diffusion throughout the breast, soon followed by enlargement of the other breast. As has been remarked, the disease may be unilateral, but the pathology of such cases is doubtful. After attaining a certain size the enlargement may cease. The growth may progress for years, or it may reach its limit within a few months. In the beginning the breasts are elastic, but as the size increases they become lax and pendulous or even pedunculated.

The nipples do not become hypertrophic, but are flattened and depressed; the areola is generally greatly enlarged; and the skin, although sometimes edematous at dependent portions, is for the most part normal and grows with the gland. Large veins course over the surface, but the axillary lymph nodes are not

implicated. Respiratory disturbance has been noted in some cases. There is seldom any pain, but decided discomfort is experienced usually due to the enormous size of the breasts, which have been known to hang down as low as the knees and to require a table to support them. The size may diminish or subside after confinement, but may again increase with the next pregnancy; and it has also been observed to lessen after marriage. Tissue resistance is low, and ulceration, abscess, and gangrene are apt to follow trivial injuries.

It occurs in both the male and the female breast (in the former being known as gynecomastia) and begins apparently oftener in the left than the right breast.

In the reported cases the age limit ranged from eleven to forty-two years.

The size of the breasts has reached enormous dimensions, varying from one and one-third pounds to sixty-four pounds, with an average of seventeen pounds, and in the case of Durston the weight of both mammæ was 124 pounds—exceeding the weight of the body after operation. The greatest circumference was fifty-one and one-half inches, and the average circumference was thirty-one and one-half inches (Albert).

Instances of remarkable development of lactation in both extremely early and advanced stages of life are mentioned by Shield and many other writers. For example, these include a woman of sixty-one years who nursed her grandchild; a child of three years whose mammæ and genital organs were fully developed; and an infant less than two years old with established menstruation and large, well-developed breasts. Mudd reports a personal case of an infant who menstruated at the age of fifteen months, and at four years and nine months the mammæ were large and fully formed.

The *prognosis* may be considered good except in the presence of general debility and emaciation, or other serious maladies.

Treatment.—In the milder cases, palliative measures may be tried, the breast being supported by a properly adjusted sling or bandage, precaution being taken against undue pressure lest ulceration and infection follow. A restricted diet, recumbency for a long period, and the administration of thyroid extract and the iodine salts have been advocated. In the gestational form the possibility of rapid subsidence after parturition should not be forgotten, and in cases of great gravity miscarriage should be induced. In the virginal and non-pregnant forms amputation is the only rational method of treatment. Both breasts can be removed at the same sitting, but it is often wiser to allow an interval of several weeks to intervene before operating on the second organ.

Hemorrhage is usually excessive, and the bloodless method of amputation by Wyeth's pins and elastic constriction should not be neglected.

Porter has reported operating on sixteen cases without a death, and Williams collected twenty-two operations with only one death.

Senile Parenchymatous Hypertrophy.—This hypertrophy is a most interesting affection of striking importance and is due to parenchymatous changes in the female breast occurring just prior to or during the climacteric state. It has been described under a great variety of titles which fully attest to the marked difference in the conception existing as to the pathology of the disease: It was designated chronic cystic mastitis by Koenig; cystadenoma by Schimmelbusch; chronic cirrhosing mastitis by Billroth; chronic mastitis or diffuse fibroadenoma by Wood; fibrous and glandular hyperplasia with retention cysts by Whitney and others; interstitial mastitis by English writers; abnormal involution by Warren; and senile parenchymatous hypertrophy by Bloodgood. Thus, as would be inferred, the earlier investigators attributed it to the result of distinct inflammatory changes; then came Schimmelbusch and contemporaneous writers who believed that it represented a true neoplasm with cyst-formation; and finally American surgeons, chiefly Warren and Bloodgood, who regard the process as an abnormal involution producing a definite hypertrophy of the parenchyma, and which is now the more generally accepted theory. Therefore it is to be considered as clearly a lesion of the senile breast, especially occurring between the ages of forty and fifty years, and is more commonly found in unmarried women and married women who are sterile or who have borne children but never lactated. It appears distinctly

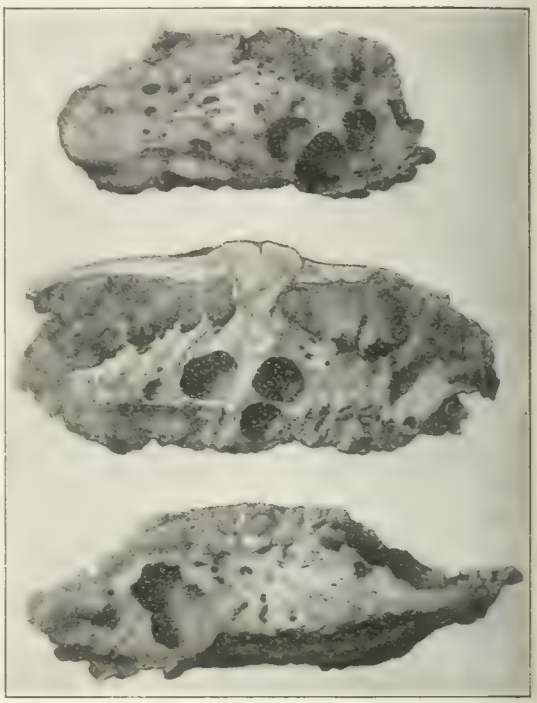

Fig. 1114.—Abnormal Involution. "Chronic cystic disease," "chronic cystic mastitis," gross appearances. (Warren, American Journal of the Medical Sciences, April, 1907.)

within the cancer period, and as it is prone to malignant transformation the possibility of such a transition is of great importance, and should be kept prominently in view by the surgeon. The frequency of carcinomatous degeneration has been variously estimated at from ten to fifty per cent. Warren found carcinoma either coincident with or resulting later in thirteen per cent., and Greenough and Hartwell in their series of cases place it at ten per cent. A previous mastitis is said to be a predisposing cause.

There are a few rare instances on record where senile parenchymatous hypertrophy accompanied by cyst-formation has been encountered in the male breast. These cases presented all the characteristics of the disease as seen in the female mamma.

Pathology.—The disease is divided into a benign and a malignant stage. The benign stage has two recognized types, the cystic and the adenocystic.

In the *cystic type* the distinguishing feature is the presence of cysts without proliferative epithelial changes—the fibrous thickening having produced ectasia or dilatation of the ducts alone. These cysts are generally multiple, both large and small, and with smooth walls. At first they are lined by one layer

of columnar epithelium, but later with the increase of pressure from the retained secretions, this epithelial lining is lost. The cysts contain a turbid, brownish, or greenish fluid, but it is never bloody in character.

The *adenocystic type* is characterized by the existence of cysts together with proliferative epithelial changes. This epithelial growth is observed in

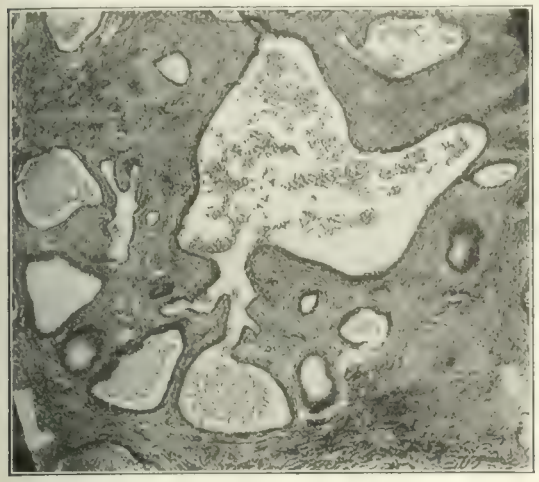

Fig. 1115.—Abnormal Involution; Cyst Formation. Microscopic appearances. (Greenough and Hartwell, Journal of Medical Research, Vol. II, Plate 21, June, 1903.)

several degrees, as proliferation of the acini, papillary outgrowth of the epithelium into the cysts, and adenomatous epithelium multiplication. Hence, in some varieties of this type there is evidence of a recent subacute inflammation, both the periglandular connective tissue and parenchyma showing such changes. In other instances the adenomatous quality is more prominent. The cysts and glandular acini

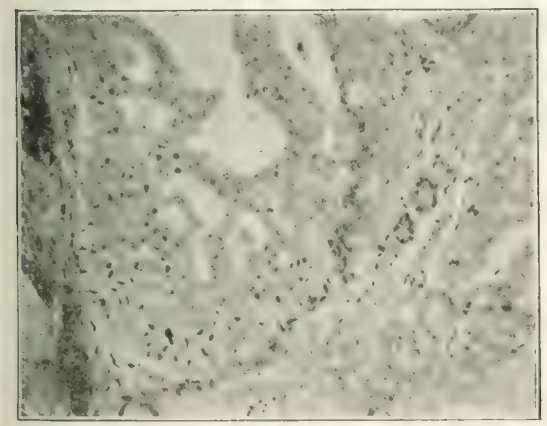

Fig. 1116.—Abnormal Involution; Microscopic appearances. Papillary and adenomatous types of epithelial proliferation. (Greenough and Hartwell, Journal of Medical Research, Vol. II, Plate 22, June, 1903.)

are filled with cells and epithelial débris due to cell proliferation from their walls, or to a papillary outgrowth resembling an adenoma.

The malignant stage represents the transitional period from the adenomatous to the carcinomatous. Here the pathological condition is identical with adenocarcinoma.

In gross appearance it is quite the picture of a cystic adenoma with the exception that it is diffuse and not encapsulated. The interlobular connective tissue is distinct; papillary ingrowths are frequently seen; but the notable features are ectasiæ or dilatations of the acini and the ducts.

Its early recognition is of the highest importance. Bloodgood has shown that the closer the pathological condition approaches the adenomatous, or adenocystic, type, the more prone it is to cancer development. But on the other hand, where the tendency is to the formation of a single large cyst or multiple smooth walled cysts, carcinomatous transformation is infrequently encountered.

Symptoms and Diagnosis.—One or both breasts may be implicated. It rarely begins in a single area, but ordinarily originates in several points or areas of the same or both glands, and becomes diffuse and involves the greater part of the breast. When thus forming multiple hardenings in both mammæ, where in a senile breast an atrophic condition is naturally to be expected, the diagnosis should not be difficult. If only a single portion or quadrant of the breast is involved, the lengthening of the diameter of the affected quadrant is stated to be of diagnostic significance.

Palpation of the hypertrophied area usually discloses a more or less well-outlined mass, rather hard and firm, but it may be fluctuant. This mass is without intimate skin or fascial attachments; it is tender to the touch, but the color of the skin is not changed; and in many cases pain is quite pronounced, and increased at the catamenia. As a rule there is neither inversion of nor discharge from the nipple, and the fat is not atrophic. Where, however, cancerous degeneration has taken place, nipple retraction is usual. The axillary lymph nodes may be hyperplastic but are soft; and metastases do not occur before the advanced malignant stage.

Treatment.—The surgeon should keep in mind the fact that the condition is primarily benign, and may continue unchanged for quite a long interval of time. But even at an early period it is impossible to say whether or not malignancy has supervened, and hence an induration in the breast of a woman at or during the menopause must be regarded with suspicion, and the breast had better be excised. A plastic resection may be made and the growth removed for immediate examination, and then, if indicated, this can be converted into the radical operation for carcinoma.

Partial resection is not to be advised save in exceptional instances, and the same may be said of aspiration under aseptic precautions, although this simple procedure has occasionally resulted in cure in single cysts. Medical measures have no place in the treatment.

Elephantiasis of the Breast.—This is an extremely rare affection of the breast, and consists, as it does elsewhere in the body, of an enormous hypertrophy of the skin and subcutaneous areolar tissue. Elephantiasis is sometimes found in temperate regions, but it is a very common disease of tropical and subtropical countries. Obstruction of the lymph channels by one or another means is responsible for the hypertrophic tissue changes, a frequent cause of which being the *Filaria bancrofti* and its larvæ. These nematodes, by accident or through an error of instinct, on rare occasions may enter the lymphatics of the upper portion of the body, including the breasts. It is the opinion of some observers that repeated local inflammatory disturbances are a necessary part in the production of elephantiasis, but this belief is negatived by a number of reported cases in which inflammation was at no time present. The simple obstruction of the lymph ducts of the part involved seems sufficient to produce the condition.

When the breast is affected, complete excision of the

gland with removal of the axillary lymph nodes is the treatment called for.

Gynecomastia (*Gynecomazia*).—The actual definition of the term gynecomastia signifies an excessive size of the male breast, and was employed by Paul d'Egine to designate the male breast possessing the dimensions and functional characteristics of the female breast. It was believed that under certain conditions the male mammary gland was in fact capable of secreting milk and assuming the rôle of the female organ, and the literature of olden days abounds in recorded examples where this was stated to exist. In modern times, however, reports of such cases are rarely found, and among scientific physicians the existing opinion is that such a condition is, to say the least, most improbable. More than that, as Woodyatt remarks, there is no authentic instance where the milk from such a source has been subjected to proper chemical and microscopic examinations. In addition, it has not been shown that the acini of such glands are developed to the same degree as those of the lactating female breast; and it is probable that the milk-like fluid that frequently exudes from the nipple of these breasts is derived from a cystic formation, or is of a purulent character. It is true that the mammary glands of the male and the female are identical in structure up to the period of pubescence, and that the so-called mastitis adolescentium occurs in both sexes; but from that time the resemblance ceases, the male gland remains stationary, retaining its rudimentary features, whereas the female breast continues to increase in outward size and glandular development, preparatory to entering upon the destined function of lactation.

It has been clearly demonstrated by Volkmann, Scheiber, Israel, Stieda, and others, that the condition of gynecomastia is purely an hypertrophy, and that the enlargement may consist in an increase in the fibrous stroma and parenchyma, or be due exclusively to the excessive production of adipose tissue. It is mentioned by Dennis that the affection is very prevalent in Pomerania. But it now seems to be rare in all countries, and Puech has shown that only one case was discovered among 13,000 French conscripts.

Two varieties are described, namely, one in which the sexual organs are normal; and the other in which the testicles are defective, either congenitally or from traumatism or disease. In the former type Williams considers that the condition is caused by a reversion to that early state when both the male and the female parents suckled their young. The enlargement commonly begins near the time of puberty, and generally involves both glands; but it is often unilateral, the left breast being more frequently affected.

In the second type, congenital anomalies, particularly some form or degree of hermaphrodism, are connected with the mammary hypertrophy. Gigantism of the upper extremity on the same side also may be an associated anomaly. When castration is performed during the stage of highest sexual activity, hypertrophy of the mamma may result; but when this operation is executed before puberty or on men toward middle age, no effect upon the breast has been observed to follow it. Certain diseases of the testicle, as for example, syphilis or parotitis, in which atrophy of the testis occurs, may be followed by gynecomastia. In gonorrhea, however, where the epididymis alone is involved, testicular atrophy is very unusual, and mammary hypertrophy has not been found connected with the malady.

No treatment is called for except in those instances where removal of the deformity is desired by the patient, when plastic resection may be resorted to.

Atrophies of the Breast.—*Pathological Atrophy.*—Various disturbances, other than those due to defects of development, may be the cause of atrophy of the mammary gland. Severe traumatism, certain infectious diseases, and inflammatory conditions have resulted in arrest in growth and subsequent wasting of the gland. Mastitis of the new-born is regarded as a particular etiological factor. The atrophy is rarely complete, and may be either unilateral or bilateral; enlargement of the breast at puberty and lactation after pregnancy fail to occur; and it is frequently accompanied by a condition of infantilism. The normal covering of fat may conceal the deformity.

Removal of the ovaries in early life has been followed by mammary atrophy, although if oöphorectomy is performed at full sexual maturity no effect upon the volume of the gland is noticed.

Certain drugs are accredited with the faculty of diminishing the size of the mammæ, especially potassium iodide. Dennis, however, relates a case of a young girl to whom large daily doses of the salt were administered for a period of many weeks, but no changes in the breast occurred.

Senile Atrophy.—Atrophy of the mamma is a normal process during the stage of involution. At the climacteric the parenchyma shrinks and disappears and is replaced by a growth of fibrous stroma and fat deposit, this condition being characteristic of the gland structure in old age. Thus, the senile breast under the microscope is seen to be composed of a fibrous tissue framework filled in with fat, which often is excessive, with a few ducts and acini scattered about. These remaining elements are very subject to cystic degenerative changes.

Diseases of the Nipple and the Integument of the Breast.—Acute affections of the nipple rarely assume importance except during the functional activity of the mammary gland. The naturally congested state of the breasts attendant upon the early days of lactation, together with the increased secretion produced by the sucking efforts of the child result in greater engorgement and milk retention. Add to this a deficiency in the development of the nipple and a want of cleanliness, and you have the essential etiological factors in the greater number of inflammatory lesions of the nipple. Platzer states that in 1,000 cases in his clinic in Budapest, he found suckling the child to be the only cause of inflammatory lesions of the nipple. Such conditions he ascribes to the combined effects of bruising by the infant's gums, traction on the nipple during nursing, and maceration of the delicate nipple epithelium produced by the mother's milk and the secretions from the mouth of the child. Badly formed nipples are more prone to be thus affected than normal ones. Primiparæ are the more frequent subjects.

It is of first importance, therefore, that the condition of the nipples be ascertained during the later months of pregnancy. When the normal protrusion of the nipple is absent, and it is small, flattened, and depressed into the areola, persistent endeavor should be made to overcome this lack of development by frequent traction with the fingers, or by the employment of some one of the many nipple suction devices. These measures should be supplemented by frequent bathing of the breast, and the application of astringent and antiseptic lotions to harden the delicate skin of the nipple and its surrounding areola. After confinement the same cleansing and hardening methods should be diligently pursued, both before and after nursing, in order to free the nipple of the germ carrying secretions of the child's mouth. Equal care, of course, should be given to the mouth of the infant.

Inverted Nipple.—The typically formed nipple is of a cylindrical shape, protrudes about half an inch or more beyond the breast surface, and is rugous or even nodular, but never fissured. There are many deviations from this standard—varying from a stunted nipple to a mere central areola depression into which the milk ducts open.

Inversion or retraction of the nipple is frequently a congenital defect—an error of development—or it may result from cicatricial contraction following disease or injury, such as burns, ulcerations, carcinoma, and like affections, and even from the pressure of tight-fitting clothing. As mentioned before, it is a most important element in the production of certain acute affections of the breast.

Carefully applied traction, together with the use of the wooden nipple shield, will remedy the condition in some instances. Operative measures have been mentioned as beneficial in a few cases of the congenital type.

Eczema.—Eczema of the nipple and areola and the skin of the breast does not differ from this affection in other portions of the body, and yields to the same treatment as applied elsewhere. It may affect one or both breasts, and may be independent of the sources of irritation connected with pregnancy and lactation. Want of cleanliness is not an unusual cause. It appears as an irregular red, excoriated area of skin about the nipple, and which is covered with crusts. The nipple and areola of the male breast may be similarly affected.

The intractable chronic forms may be difficult to distinguish from malignant papillary dermatitis or Paget's disease of the nipple.

Paget's Disease of the Nipple.—(See Malignant Papillary Dermatitis, under heading of Carcinoma.)

Inflammation of the Nipple (Fissures, Erosions, Cracks, Etc.).—Fissures, excoriations, and like affections, form the principal inflammatory diseases of the nipple and areola, and occur most frequently during lactation. They are caused by the trauma and maceration of the delicate skin of the nipple inflicted by the child during suckling. These lesions are distressingly painful, and the intense burning and smarting when the child is at the breast are far beyond the degree of inflammatory action present, and often render nursing impossible. Associated with these conditions small abscesses may form in the areola, following bacterial invasion through the atrium of the denuded derm. Scrupulous cleanliness, frequent bathing, and keeping the parts dry, together with the use of antiseptic and astringent lotions, such as acetate of lead lotion, solutions of alum, boracic acid, alcohol, painting with tincture of benzoin or a weak solution of cocaine, or the use of some drying powder, constitute the usual treatment. The nipple shield is of great assistance, and should be employed early. In severe cases weaning the child may become necessary. In cases of deep and persistent fissures the application of silver nitrate will often effect a rapid cure.

Furuncle.—Boils of the areola occur more commonly in nursing women, and are due to infection of the sebaceous glands of the part resulting in one or several small superficial, inflamed, tender, and hard nodules, which may be quite painful. These nodules soon suppurate, open, and discharge, and in some cases they may merge together and form short subcutaneous sinuses.

Abscess of the nipple is rare. Velpeau believes that it usually arises in a milk channel. Only a small quantity of pus forms, and, as this discharges, milk will often escape through the opening.

Ecchymoses of the nipple and areola, due to sucking efforts and the bruising caused by the child's gums, is sometimes observed.

Hyperesthesia and rigidity of the nipple is occasionally met with, and is probably associated with some uterine or ovarian disturbance.

Chancre of the Nipple and Breast.—The primary or initial lesion of syphilis is not very infrequent in this situation, and even may be bilateral. It has been reported in men as well as in women, although inoculation is most often acquired by suckling an infant with mucous patches in the mouth. I have personally seen two examples of chancre of the nipple, one at the base and the other on the nipple proper, in women who were bitten by their syphilitic paramours. The lesion is usually situated on the nipple or at its base, and appears as a fissure, erosion, or ulceration, and may be mistaken for simple fissure which it closely resembles. An indurated crack or sore on the nipple which is chronic and proves rebellious to ordinary local measures, associated with enlarged and indolent axillary nodes—especially located just under the edge of the pectoralis major muscle—is sufficient to make a provisional diagnosis of lues. The presence of the *Treponema pallidum* furnishes the positive answer. When a chancre occupies the skin overlying the breast it has much of the appearance of such a lesion on the genitalia.

Secondary manifestations of syphilis are here observed as mucous patches and moist condylomata of the nipple or areola, and also along the inframammary crease in pendulous breasts.

Antisyphilitic treatment should be prescribed, and the nursing child separated from its mother.

The infection of *diphtheria*, through the medium of the nipple, has been communicated from the nursing child to the mother. Such an example of a six weeks old baby with tonsillar diphtheria, is mentioned by Caddy.

Thrush may be conveyed in a like manner from the nursing child.

The integumentary system of the breast is also subject to many other affections found on other parts of the cutaneous surface, such as chancroid, lupus, keloid, scabies, erysipelas, herpes zoster, etc., but these do not call for notice here.

Tumors of the Nipple and Areola.—The most frequent growths of this locality are *sebaceous (retention) cysts*, originating in the glands of Montgomery. Cases of *epithelioma*, also arising in the sebaceous follicles, are reported.

Examples of *true hypertrophy* of the nipple, and *papillomata* and *angiomata* of the nipple and areola have been noted, and are occasionally found in the literature.

These affections occur in the male as well as the female breast.

Disturbances of Function.—*Neurosis of the Breast (Neuralgia, Mastodynia, Irritable Breast).*—This affection is more often met with in young, usually unmarried, women between the ages of fifteen and thirty years (Gross), at a time when the gland is nearing or has reached its highest development, and is intimately associated with disturbed sexual life.

Swelling of the breast with tenderness is frequent at times of uterine change or derangement, particularly at the catamenia, at the beginning of puberty, during gestation, and even at the menopause. Indeed, the slightly painful or sensitive breast is such a common attendant upon the menstrual epoch that but little heed is given it by women thus affected.

When these symptoms are intensified the condition is given the name mastodynia—painful breast—which may become agonizing, unbearable, and the cutaneous hyperesthesia often so severe as to be intolerant of a touch or the pressure of the clothing. The pain may be localized in the breast or it may shoot through the gland up into the shoulder, down the arm, and also radiate over the intercostal area—following the course of the intercostohumeral and intercostal nerves. One or both breasts may be affected.

The subjects of the disorder are usually slender and delicate women, with pale skins, and are generally of the better classes of society. They incline to the neurotic type and are often hysterical, given to brooding, dwell upon their sufferings, and frequently become depressed by the fear of malignancy. Such patients may also be subject to neuralgia in other localities, or may suffer from rheumatism.

Examination of the breast is for the most part negative, except possibly that the affected gland may be a little firmer to the feel and slightly larger than its companion. In some instances sensitive lobules may be distinguished, constituting a form of *lobular mastitis.*

The *treatment* consists in attention to the pelvic organs, regulation of the secretions, substantial food, changing the mode of life to an active, useful, out-of-door existence, together with tonics and reconstructives if anemia be present. A gouty or rheumatic tendency should receive due attention. Local applications are of little avail, but when the breasts are pendulous a supporting sling may afford comfort. The pain and hyperesthesia may be so intense and persistent that amputation of the whole breast becomes the only remedy, as occurred in a case mentioned by Finney. Resection of the involved nerves may afford relief.

Spontaneous Ecchymosis.—A rather peculiar condition of ecchymosis of the breast, non-traumatic or spontaneous in origin, has been observed in women suffering from difficult menstruation. It is often preceded by severe pain in, together with swelling of, the mamma. These symptoms may be of a mild character, but occasionally they are pronounced and may be accompanied by oozing of blood from the nipple and other distressing symptoms.

Regulation of any existing disturbance of the menstrual function, and meeting whatever other conditions that may require attention, covers the necessary treatment.

Mastitis (Mammitis).—Inflammation of the mammary gland is met with at all ages, but there are certain periods of life at which the breast is distinctly more susceptible to this process than at others, namely, just after birth, in adolescence, during lactation, and at the time of senile atrophic changes. Therefore it is customary to classify such conditions according to these several periods, to the structures involved, and the degree of inflammation.

Mastitis is comparatively rare in the male breast, since, naturally, lactation and associate conditions are absent. When it does occur, however, it usually results from traumatism or is dependent upon infection following necrosis of a rib, tuberculosis, syphilis, etc.

Acute inflammation of the breast (*mastitis acuta*) almost invariably occurs when the functional activity of the gland is at its height; whereas, the low grade or *chronic form* (*mastitis chronica*) is more apt to follow lactation, or to be associated with the waning stage or time of senile decline of the mamma.

Mastitis Neonatorum.—Inflammatory changes in the breast of the new-born child frequently accompany the hypertrophy of the organ met with at that period. The condition occurs in both sexes within the first week after birth, and is characterized by swelling, often redness of the skin, and occasionally with oozing of a turbid, milk-like fluid from the nipple. As remarked by Dennis, it may be aggravated, or possibly induced, by the manipulations of an ignorant nurse in attempting to empty the breast of the small quantity of colostrum it sometimes contains.

The cause of the disorder is a question of some doubt—even as to its being a positive inflammation. It is regarded as inflammatory by Warren who believes that the process is inaugurated *in utero*, inasmuch as he found active proliferation of epithelium and clogging of the ducts with epithelial débris, similar to a true inflammation, in the glands of new-born infants. Others (Koelliker) regard the changes as concomitant to normal development, and attribute the secretion to epithelial degeneration and crowding the ducts with débris before birth (De Sinéty), and also to a positive lacteal secretion.

This condition usually subsides in a few days, and seldom requires any treatment beyond hot moist applications or some soothing lotion. Any manipulation of the breast is officious and harmful, and may even intensify the condition to the point of suppuration. When pus is present it should be evacuated by an incision radial to the nipple, with drainage or not as circumstances require.

Mastitis Adolescentium.—At the time of puberty both sexes are subject to a form of mastitis designated by the above caption. It is more frequent in girls than in boys, and particularly in those of delicate mould, with feeble musculature, sallow skins, and irregular bowels. In mild cases the breast is swollen, tense, hard, and resilient to the feel, and small deeply seated nodules may be present; it is quite painful and sensitive; or the induration may extend to the entire gland with aggravation of all the symptoms. In the still severer cases the breast is markedly enlarged, the nipple and areola are inflamed, often with hard ridges radiating outward, the axillary glands become involved, and the pain and tenderness are intense.

A painful and enlarged condition of the breast also occurs in young girls during the catamenia, and is probably associated with sexual development. Likewise hemorrhage from the nipple, probably a vicarious menstruation, has been noted under similar circumstances.

In the male (*mastitis pubescentium virilis*) it is stated by some writers to affect the left breast more often than the right; and also when the inflammation continues for a long period of time it may produce a permanent enlargement of the gland.

The symptoms gradually decline without treatment, and after several weeks the breast regains its normal state. Resolution is hastened, however, by carefully adjusted pressure, warm and moist applications, or soothing salves. Suppuration rarely occurs, but when abscess forms, evacuation of the pus should be effected.

Chronic Interstitial Mastitis.—There is a chronic form of mammary inflammation of rare occurrence which is observed during or near the menopause. It consists of a dense fibrous infiltration and atrophy of the breast and its superimposed fat, and has been termed "cirrhosis mammæ." It is evidently an interstitial inflammation, and two forms are recognized, a diffuse form and a circumscribed form. The resemblance to scirrhus cancer is very positive, and may be confused with this malignant growth. Therefore the differential diagnosis is extremely difficult, often impossible, and then often cleared up only after exploration or removal. Surgical intervention is called for.

Chronic forms of mastitis are sometimes met with in the male, and may be of syphilitic or gouty origin, or may arise from adjacent disease. Leudet has described a peculiar form of chronic hypertrophy of the male breast connected with tuberculosis of the lung on the same side. This mammary enlargement is distinctly inflammatory and not tuberculous, and is interesting as being associated with the pulmonary disease.

Traumatic Mastitis (*Mastitis Traumatica*).—Certain injuries to the breast are known to produce an inflammation of its tissues. In men such traumatisms may be directly inflicted by means of the tools employed in their vocations, as in the case of carpenters by the brace and bit. An abrasion of the skin may then furnish a ready atrium for the invasion by infecting organisms, and suppuration results; or the mastitis may assume a chronic form with the usual attendant symptoms.

Puerperal Mastitis (*Lactation Mastitis*).—It is well known that ordinarily during gestation and the period of lactation the mammary gland, with the exception of infections, possesses marked immunity to disease. Inflammatory conditions, however, are frequent, and

puerperal mastitis is the commonest variety of the infective inflammations of the breast. It is stated to supervene in six per cent. of all nursing women (Guleke), and is especially frequent in primiparæ. Winckel states that 67.6 per cent. of all cases of mastitis are found in first lactations. However, such percentages are largely influenced by the medical attention given the patient during gestation and after parturition, and thus are shown to vary from 0.54 to 41.1 per cent. by Rubeska's statistics gathered from various German clinics (Whitridge Williams). The right breast has been stated to be more liable to the disease than the left one, and also that a preference is shown for the lower and outer quadrant.

The degree of inflammation ranges from a simple state of congestion and milk retention to the severest suppurative type.

During the last days of pregnancy and in the first seventy-two hours of lactation the breast often becomes largely distended, firm, and knotted on palpation, which is frequently accompanied by much pain together with a slightly elevated temperature and accelerated pulse. Only a portion of the gland is involved, the trouble being usually confined to a single lobe. This condition is vulgarly termed "caked breast," but technically is known as *stagnation mastitis*. It is ordinarily of brief duration and subsides either spontaneously or yields to the application of gentle massage, supportive and compressing bandages, the ice bag, and the use of the breast pump—measures designed to empty the breast of its retained secretion and relieve the surcharged state of the blood-vessels. Should such treatment fail to bring about resolution, it may be advisable to dry up the milk in order to avoid suppuration, which invariably succeeds upon a continuance of this condition.

In those instances where the symptoms are not speedily relieved, but continue unabated, the excessive distention leads to mild tissue changes in the glandular elements with lessened resistance. Microbic invasion now soon follows with resulting suppuration, and an infective or pyogenic mastitis is inaugurated.

This parenchymatous inflammation of the breast is the commonest form, and not an infrequent complication of the puerperal state. It follows, and usually is an extension of, the engorged condition just described. The symptoms generally become manifest from the end of the first to the fourth week after labor, and are ushered in by the ordinary signs of beginning infection.

Etiology, Symptoms, and Course.—This form of mastitis is always due to the invasion of pyogenic bacteria by way of abraded or fissured nipples, through the avenue of the lymph vessels, or by the lactiferous ducts, in which latter channels bacteria are usually present, ready to assume virulence as conditions may favor. The infection may also spread from surrounding structures, such as the subareolar area and the neighboring sebaceous glands. Hönigmann, Bumm, and Koestlin, together with other searchers in this field, have shown that the staphylococcus pyogenes albus and aureus are found in from eighty to ninety-four per cent. of all mammary glands. Under natural surroundings these bacteria are innocent residents of the lacteal fluid, but they take on pathological activity with the tissue changes incident to engorgement and imperfect drainage. The streptococcus has also been found in these cases, and even the presence of the gonococcus has been demonstrated—the infection following direct inoculation from the vagina of the patient or by the gonorrheal pus from the eyes of the nursing infant. Mastitis has also been ascribed to the infection from puerperal metritis.

The virus seems to follow the perilobular lymphatics and then spread out through the anastomosing lymphatics in different directions. At first it is probably limited to the immediate vicinity of the gland structure, since in the beginning the interstitial connective tissue is practically free of infection; but later it may extend to the deeper structures, attacking and destroying the greater part of the gland. In other and favorable instances the process is less severe, and may end in final resolution and without damage to the breast.

The symptoms are those usually attendant upon suppuration; and when the surgeon does not interfere, but which he should always do, the process goes on to softening and spontaneous evacuation of the pus. When the infection enters through the atrium afforded by excoriated or fissured nipples, the character of the inflammation is usually of the phlegmonous type.

The abscess (*suppurative mastitis*) may be located superficially, in the subcutaneous tissues of the breast, forming a para- or supramammary abscess, or limited to the subareolar space with the formation of a small abscess, which has been spoken of as *subareolar mastitis*. When the abscess occurs within the lobules it is designated as intramammary; and if the infection burrows backward into the loose cellular tissue beneath the breast a retro- or submammary abscess may result. In the superficial and intramammary varieties the bacteria travel through the lymphatics connected with the affected nipples, or by the route of the lacteal ducts; but the submammary form of abscess arises secondarily from the infected breast or the adjacent thoracic wall or cavity. Purulent collections within the breast structure may be single or multiple—one large abscess or numerous small ones, which latter may coalesce at a later stage. If not incised the pus may tunnel its way to the surface by one or more openings, leaving intractable sinuses. The process may be so extensive that the gland is completely destroyed, functionally and otherwise.

The symptoms consist of a tense, firm swelling of the breast, either a circumscribed or diffuse induration, tenderness, and a constant throbbing pain, with redness and infiltration of the skin in the later stages. Fluctuation is often difficult of detection. When the abscess is retromammary the symptoms are not so characteristic, and the whole breast is thrust forward and bulges as a firm, tense mass.

The immunity of the mamma to disease during lactation has already been mentioned, the chief exception being that of infection. But this statement should be qualified, for, in rare instances, malignant tumors of the breast may develop during pregnancy and the nursing period. Bloodgood believes that an induration in the breast occurring before delivery in women over twenty-five years of age, should always be explored, and states that in his experience it is either carcinoma or tuberculosis. He has observed eight cases of carcinoma and two of tuberculosis in the lactating breast. Finney observes that carcinoma developed during lactation in two per cent. of the cases in Halsted's clinic.

Treatment.—The treatment of puerperal mastitis should begin with its prevention. By needful and appropriate attention given to the breasts during the last months of pregnancy and after parturition, abrasions and fissures of the nipples, the chief cause of mastitis and abscess, can be largely prevented, and nursing rendered more comfortable for both mother and child. To this end the breasts should receive frequent and cooling baths, a light supporting bandage adjusted if they be heavy and tense, and applications to the nipples of hardening and antiseptic lotions made several times daily, such as a saturated solution of boracic acid in equal parts of alcohol and sterile water, or a similar solution to which has been added borax and alum. These measures afford the very necessary cleanliness, toughen the skin, and

render the nipple more resistant to the traumatisms of nursing and other outside influences.

If the nipples are small and depressed, attempts should be made to draw them out and bring about their development by frequently applied traction, together with wearing the wooden nipple shield for several hours during each day. When the nipples are deeply inverted every means to rectify the deformity may fail.

After labor and during lactation these measures should be persisted in, and, at the same time, equal attention should be paid to the child's mouth before and after each nursing, since the buccal cavity has been shown to contain pathogenic bacteria in ninety-eight per cent. of infants at the time of birth (Kneise). When the breasts become engorged and in the early stages of mastitis, the condition should be met by applying a firm compressing bandage and an ice bag, together with the use of the breast pump and careful massage to remove the secretion, and the usual attention to the nipples continued.

Where abscess has developed, too much stress cannot be placed on the necessity for early evacuation by one or more incisions radiating from the nipple, but, if possible, avoiding the areola. When the abscess is small and confined to a single lobe only a short cut is required, and this can be done under local anesthesia; but the mistake must not be made of making an insufficient opening with consequent defective drainage. If this be neglected the suppurative process is liable to spread to other lobes, and the breast is in danger of partial or complete destruction. Where the abscess is large, free incisions should be made, under general anesthesia, through each softened area. These openings may be supplemented by another incision in a dependent portion of the breast, or beneath the gland through the inframammary crease, burrowing up with forceps to the abscess cavity and draining it from the base. The finger should be passed into the openings, the septa broken down and the several pockets converted into one large cavity, then curetted if desired, and followed by the introduction of ample tubular drains.

Recently the Bier hyperemia treatment for acute infection has been employed in suppurative mastitis with gratifying success. B. M. Bernheim has given the method extensive trial, and his conclusions are, that there is almost absolute freedom from pain during the course of treatment, that the gland function is better preserved, a minimum of scar deformity is left, a distinct shortening of the disease is obtained, and, in cases seen early, the prevention of abscess formation.

In severe cases with extensive and multiple abscesses, associated with serious general infection, amputation of the breast may become necessary.

Chronic Lactation Mastitis.—A chronic form of mastitis is recognized as connected with lactation inflammation of the mamma. In fact it seems very desirable that the term chronic should be limited to these cases alone, since, if so applied much of the existing confusion connected with so-called chronic mammitis would be eliminated.

This condition is found toward the end of lactation, and is characterized by numerous small abscesses and necrotic foci scattered throughout the breast in intimate relationship with the deeper ducts. These small pus formations are observed as hard masses, sometimes adherent to the skin, and the axillary glands may be hyperplastic. The fibrous tissue is increased, and the periductal tissue is infiltrated with leucocytes and small round cells. The distinguishing clinical features are the extensive induration of the breast, irregular in character, and found especially in young women late in lactation. Bloodgood mentions two cases with chronic abscess. The treatment is entirely surgical.

Mammary Fistula.—One or several fistulæ communicating with the surface of the breast or with the pleural cavity, may follow prolonged suppuration of the mammary gland. These fistulæ sometimes heal spontaneously, but oftener are intractable and require free incision, curetting, and gauze packing for their cure.

Pyogenic Mastitis.—The highest type of pyogenic mastitis is represented by that variety associated with and characteristic of the lactating breast, but the present heading is intended to cover that form which occurs independently of the puerperium. Such sources are found in certain specific infections involving the structures adjacent to the breast, that is, pyogenic diseases of the ribs, axilla, or arm, and in typhoid fever. Bloodgood observed six cases among at least 1,200 diseases of the breast. Davis records a case resulting from typhoid fever on the thirty-ninth day of the disease, in which the pus aspirated from the gland grew a pure culture of the typhoid bacillus. H. Roger reports a personal case of suppurative post-typhoid mammitis, and was able to collect twenty-three additional cases. In one of these the disease was bilateral, in one it coexisted with thyroiditis, and ten of the twenty-four cases suppurated. He states that it usually appears during the decline of the disease and less frequently during convalescence.

Free incision and drainage in the suppurative cases, and a rational treatment for the non-suppurative ones, are called for here as in other forms of mastitis.

Postmammary Abscess (Submammary or Retromammary Abscess).—The pus in suppurative mastitis finds, as a rule, the least resistance to its progress in an outward direction, and in consequence it commonly approaches the surface on the anterior aspect of the breast. But in some cases the pus makes its way backward into the loose retromammary cellular tissue, where it collects and forms a postmammary abscess. In other cases the infection has its origin in tuberculosis or osteomyelitis of the ribs or their cartilages, in typhoid periostitis, and from injury; or pus from an empyema may penetrate the chest wall and accumulate in this location. Abscess is rare in the male breast.

Treatment.—A large incision and free drainage should be practised. The incision should be made along the dependent edge of the breast, with preference given to the Warren plastic resection method by which the abscess cavity is easily reached. This incision is particularly applicable to those cases complicated by disease of the thoracic wall and cavity, when any additional operative work can be carried out at the same time.

Specific Infections of the Breast.—There are three particularly important specific infections or inflammations of the mammary gland, namely, (1) syphilis, (2) tuberculosis, and (3) actinomycosis.

(1) *Syphilis (Syphilitic Mastitis; Gumma).*—Syphilis may involve the mamma, and produce both an acute and chronic inflammation of its tissues. It is relatively rare, and may be confused with carcinomatous infiltration. The primary lesion or chancre, affecting the nipple, together with certain manifestations in the skin of the breast have already been dwelt upon.

Affections of the gland itself should be grouped among the late secondaries, or the tertiary forms of the disease, although it may occur quite early in the secondary period; for, like many late manifestations of this erratic infection, it may sometimes desert its regular rank for an earlier one. Thus an *acute mastitis* may be seen during the early constitutional stage, accompanied by swelling, pain, and tenderness. Cases of this character are recorded by Ambrosali and others.

The more common exhibitions are the *gummatous* and the *diffuse infiltration types*. In the first stages of gumma it may appear as an insensitive, ill-defined, roundish infiltration, unattended by either adenopathy or other positive symptoms, which closely

simulates a malignant growth. Somewhat later this becomes more circumscribed, and pain and tenderness may supervene. If the mass originates in the center of the gland the nipple will become retracted. At a still later period the gummatous deposit may, if near the surface, break down, implicate the skin, and produce a typical, sharp-edged, non-proliferating ulcer, with enlargement of the axillary glands from mixed infections. If the deposit be deeper in the gland, softening may be followed by a chronic or cold abscess.

Syphilitic lesion of the breast may also develop as a dense, often diffuse, infiltrated enlargement of the mamma, *a true syphilitic mastitis*, affecting one or both glands, and sometimes resulting in contraction and atrophy of the involved structures.

Syphilis of the mammary gland occurs in both men and women, and also it may be hereditary and congenital.

Diagnosis.—The diagnosis may be perplexing, and the physical signs especially hard to differentiate from cancer and tuberculosis. Furthermore, syphilis of the breast is sufficiently rare not to be suspected. A careful analysis of associated symptoms will be often necessary. A history of syphilis, or, possibly, the presence of specific lesions elsewhere, together with the absence of enlarged lymph nodes; and later the effects following the therapeutic exhibition of salvarsan, or mercury and the iodides, should in most cases clear up any existing doubts. But the information derived from the serum diagnosis by means of the Wassermann reaction or as modified by Noguchi, as well as the microscopic disclosure of the specific *Treponema pallidum* in the tissues of or discharges from the growth, afford diagnostic methods both scientific and exact.

When the presence of pus complicates the case, it may be probably differentiated from a tuberculous abscess by the absence of the characteristic tuberculous membrane. Von Pirquet's skin test may strengthen the diagnosis.

Treatment.—This constitutes the specific therapeusis of syphilis in general, that is, the judicious exhibition of mercury and the iodine salts, with or without the injection of salvarsan. Where the lesion is an old one and resistant to medicinal treatment, operative intervention may be required.

(2) *Tuberculosis.*—As W. Roger Williams remarks, tuberculosis of the mammary gland is a disease which in recent years seems to have undergone a rediscovery, since Cooper in 1829, Nélaton a decade later, and Velpeau in 1854, published admirable descriptions of the affection—the work of Velpeau being the equal in lucidity and accuracy of any modern dissertation on the subject. Even with the later writings of Billroth (1880), Dubar (1881), Mandry (1891), and many others, the disease is still spoken of as rare in occurrence. A rather careful examination of the literature, however, would indicate that the disorder is gaining more widespread recognition, and that it occurs much more commonly than was formerly believed. There is scarcely a doubt that very many cases pass unrecognized. J. Collins Warren believes that probably the majority of cold abscesses of the breast are tuberculous. In 1898 Levings collected fifty-seven cases, of which seven were his own, all then found on record. Later an analysis of 1,500 cases of diseases of the breast in St. Bartholomew's Hospital gave only 1.5 per cent., as tuberculous; and more recently Bloodgood mentions twenty cases, the entire number up to that time which had been admitted to Halsted's clinic, all of them far advanced and necessitating amputation of the gland.

The condition is decidedly more common in the female than in the male, as shown in Mandry's collection of forty cases, in only one of which the male breast was affected; and the interval between the years of fifteen and forty, especially after twenty, appears to be the age period of preference, although it has been observed in an infant of one year, and in two women of fifty-three and fifty-seven years respectively. The disease is oftener unilateral, but both breasts may be implicated.

The malady may be primary or secondary. In the former the specific organism may gain access to the gland through abrasions or fissures of the nipple, or directly by way of the milk ducts, or by the lymph-vessels of the nipple. In this manner infection may be conveyed from the mouth of a tuberculous child.

In the secondary form the lymphatics and the blood-vessels are the accepted avenues of transmission (Roux). Halsted states that there is a retrograde transmission through the lymphatics from tuberculous axillary glands or intrathoracic deposits. Osteomyelitis of the ribs or sternum or a tuberculous empyema may be the primary focus from which the bacilli are transferred; or a like transference may take place from a greater distance, as a primary bone lesion in the extremities. A chronic mastitis may be a predisposing factor. Von Eberts reports a case of solitary or primary lesion of the breast developing upon the cicatrix of an ancient mastitis, where there was an area of induration with central abscess. The breast was not otherwise involved. The macroscopic examination of the removed specimen showed numerous typical tubercles. In this connection the case of A. B. Johnston is interesting, where a rapidly growing intracanalicular fibroma was associated with the presence of miliary tubercles. The growth was hard, and attached to both the skin and underlying deeper structures, and the axillary lymph nodes were tuberculous and caseated. It was assumed that the tuberculous infection was secondary to the fibroma, gaining entrance through the nipple.

Scudder states that fully one-half of the reported cases were in women who had borne children. Bloodgood is of the opinion that, contrary to the general belief, the onset of mammary tuberculosis is infrequent during lactation.

The primary type is the less frequent of the two, but beyond question more frequent than heretofore recognized. A number of cases of this variety are scattered throughout the literature. Von Eberts, writing in 1904, states that between that date and the publication of Dubar's monograph in 1881, there had been reported forty cases answering to the solitary type. Four out of five cases published by Kamamura in 1904, were of primary origin. But authors generally are agreed that the disease is oftener secondary to the presence of tuberculosis elsewhere in the body.

Symptoms.—The clinical manifestations of the disease are various, and it is essentially chronic in its course. Pain may be present though by no means constant. The breast may be enlarged, but, as a rule, it is small and sometimes shrunken, with palpable, fairly circumscribed, deep-seated nodules, usually situated in the upper and outer quadrant, which later may coalesce into a single irregular mass. Such a mass, or masses, gradually develop in size and in time disintegrate, resulting in softening areas covered with discolored skin, which eventuate into tuberculous abscesses, and the breast becomes perforated with numerous discharging sinuses. Suppurating glands may exist in the axilla. The breast is usually movable on the subjacent structures, but the nipple is often retracted. The axillary lymph nodes are practically always involved and caseous, although they may not be palpable. In cold abscesses, which occur in a limited number of cases, the overlying skin often remains normal. These progress slowly, may continue at a stand-still indefinitely, but in the end they gradually enlarge and become tense and fluctuant. Incision gives vent to the well-known flaky pus, and, as Halsted states, the cavity is lined with a characteristic membrane.

Diagnosis.—The diagnosis is not always clear, par-

ticularly in the early stages and if the lesion be primary. Later, after the disease has advanced and discharging sinuses have formed, the clinical picture is one easily recognized. In secondary cases, the presence of tuberculosis elsewhere is of valuable aid in the differentiation. The existence of the tubercle bacilli in the discharges and the tissues, together with cultural methods and inoculation experiments, should decide any specially obscure case. Scudder, and Gautier (Schley) have shown, however, that in primary tuberculosis of the breast the bacillus may not be found in more than one-third of the cases. The prognosis will depend upon the extent of the disease, and whether primary, or secondary to disease in other organs, more especially in the chest area. A primary lesion involving only the breast and the lymph nodes of the axilla is to be regarded in a decidedly more favorable light than when there is dissemination, and the pulmonary and other important organs are affected.

Treatment.—In primary cases, small and isolated nodules and abscesses may occasionally be treated by enucleation, incision and curetting, and the application of iodoform. But if the disease is diffuse and extensive, amputation of the breast together with a thorough dissection of the axillary glands should be performed. Possibly it might be the wisest course to remove the breast in every case, since any small tuberculous focus that is left, or an unsuspected axillary gland, may infect the mediastinal glands and the lungs.

In the secondary form the diseased breast should be excised, if the state of the patient's health admits of it and the original tuberculous process is not too extensive.

(3) *Actinomycosis.*—Actinomycosis is among the very rare diseases of the breast. Only a few cases of the affection are on record; these varying as to age from twenty-two to thirty-five years. It does not differ in its manifestations in this region from the disease elsewhere, and is a destructive process, chronic in its course, which finally results in the undermining and destruction of the gland, with resultant abscesses and sinuses. It may be primary in type, or secondary to infection in adjacent parts—in the latter case usually advancing from the lung or chest-wall to the structures of the breast.

Primary actinomycosis of the mamma at first appears as one or several nodules or masses, hard and well outlined ordinarily, not adherent to contiguous structures; it is without pain, and often only accidentally discovered. As a rule, except in the late stages, the general health is not impaired; and the axillary glands remain uninvolved which fact is a valuable aid in distinguishing it from carcinoma and tuberculosis, for which it is most apt to be mistaken. After abscess and sinus formation the diagnosis should be easily made by the presence of the fungus granules in the discharge.

Complete removal of the breast and all surrounding infected tissue is to be recommended, to be followed by the administration of potassium iodide in massive doses, and the use of the sulphate salt of copper after the method advised by Bevan. Just here it should be noted that MacArthur not long since reported a case of mammary actinomycosis where the iodide of potassium was of no avail after being administered in large doses, and which eventually necessitated total extirpation.

Injuries.—Repair of the tissues of the mammary gland after injury takes place as readily and smoothly as it does in other structures of the body.

Incised and penetrating wounds are frequently attended by free parenchymatous hemorrhage, which is easily controlled, and, unless infected, they heal rapidly, as is daily observed by the surgeon operating on this organ. If infection and suppuration takes place the same surgical measures should be employed as in similar conditions in other situations.

Contusions or injuries resulting from blunt force often cause blood extravasation into both the subcutaneous and glandular tissues. These effusions are slowly absorbed, and may remain to form hematoma with cystic limitations; or the tissues may become infected to be followed by mastitis and the formation of pus. The rôle played by contusions and like trauma in the etiology of malignant growths of the breast offers a question of much doubt. Many surgeons, to say nothing of the lay mind, are thoroughly imbued with the belief that such injuries are positive predisposing factors in the causation of both carcinoma and sarcoma of the gland, but which the actual facts would scarcely seem to warrant.

Milk fistulæ, and other chronic sinuses, sometimes follow injury inflicted during the functional activity of the gland, as, for example, contusions, penetrating wounds, and abscess formation. Such conditions should be treated by prompt withdrawal of the child from the breast, together with the employment of whatever surgical measures the individual case requires.

Burns and scalds are occasionally met with here, but call for no particular notice, except inasmuch as the resulting scar displaces or distorts the nipple, which may or may not offer, according to the degree of injury, an impediment to the outflow of milk in later confinements. Ulceration may destroy the nipple, however, in which event mastitis will invariably develop with each subsequent lactation.

Foreign bodies are not infrequently found embedded in the gland substance. Instances where needles, pins, wood slivers, sequestra from the ribs, and such like materials have been removed from the breast, often with the history of a long local residence, are scattered throughout the literature. All such bodies should be promptly removed.

Cysts of the Breast.—The mammary gland is subject to a variety of cysts and neoplasias associated with cystic formation, and clinically it is often a matter of some difficulty to separate the true cyst from that due to the breaking down or cystic transformation of solid growths, of which the cyst is only an incident. This difficulty is more especially encountered in large cysts, which may quite overshadow the original growth from which they are derived, and thus offer to the surgeon an obstacle to diagnosis that is often not easily set aside. It is the true cysts, those that are independent in their origin of other morbid growths, that we wish now to consider. They are of rather infrequent occurrence, and form about 2.6 to 3 per cent. of all mammary tumors.

Cysts of the male breast are relatively of frequent occurrence, and the annals of medicine abound in records of such cases both as to numbers and varieties.

Simple Cysts (Involution Cysts).—These growths as a rule occur in the breasts of women past the age of forty years, that is, about the climacteric. They may occupy one or both breasts but not to the same degree, and may constitute a single tumor although multiple tumors are oftener present. These formations are more common in women who have never lactated, and they compose fully one-half of all growths found in such functionless glands.

Involution cysts have been found in the male breast. J. A. Williams, Morgagni, and other writers have described such cases, and Schuchardt states that they are comparatively common in men between the ages of fifty-five and sixty-one years. These cysts may be seated in any portion of the organ, but large single cysts are more often situated toward the center of the breast whereas the small multiple tumors are found in the periphery of the gland.

During the involution period of the mammary gland the acini rapidly disappear until the parenchyma has been absorbed, leaving behind the lacteal

ducts with only traces of atrophied acini at their terminal portions. The interstitial connective tissue contracts during this process, distorting the ducts, separating the smaller ducts from the larger tubes, which thus become obstructed and dilated (ectasic) and form large numbers of minute nodules easily discerned in the breasts of elderly women. This may be considered a normal process; but not infrequently these cystic changes advance farther and some of the cysts enlarge to the proportion of a walnut or an egg, while the gland generally is also filled with myriads of smaller cysts varying in size from a bird shot to a pea. These are of a bluish color, as seen in sections of the breast. The contents are greenish or coffee colored, and contain disintegrated blood corpuscles, degenerated cells, and cholesterin crystals. The walls of the smaller cysts are lined with one or two layers of low columnar epithelial cells, but those of the larger cysts are composed of inflammatory fibrous tissue. There is a difference of opinion as to the origin of these cysts—whether they arise from the acini or the smaller ducts—but it is probable that the latter is the actual source. The presence of active epithelial cell proliferation created the view that the disease is an epithelial growth; the growth of connective tissue suggested the theory of a chronic mastitis with retention cysts. But it is more probable that the affection is an aberration of the process of involution, and that inflammatory changes in the connective tissue and epithelium are accidental (Warren).

Pain is not a positive feature, but it may be quite prominent if the tumor is of rapid growth. A discharge of a yellowish or bloody fluid from the nipple is occasionally observed, but the nipple is not retracted and there is no dimpling of the skin unless inflammatory changes have taken place in the cyst. If the tumor is superficially located fluctuation is ordinarily apparent, although often the cyst wall is so tense as to appear solid. In cysts deeply located only an indurated area is discernible. The contour is generally smooth, round, and regular. The subcutaneous fat is unchanged and the breast is of normal appearance.

The course of the disease is usually a benign one. The cysts grow slowly up to a certain size, then cease to enlarge, and commonly produce no material

Fig. 1117.—Plastic Resection of the Breast for Cystic Disease. First incision. (Warren, Annals of Surgery, June, 1902.)

trouble. But it should always be borne in mind that carcinomatous degeneration is a possible late accession.

Diagnosis.—The diagnosis may present decided difficulties. The contour, consistency, slow development, multiplicity of tumors—one, possibly two, of moderate size, with a number of smaller nodules scattered throughout the breast—and the result of exploratory puncture compose the clinical evidence of most importance. The cyst is usually a firm, tense, and distinctly defined tumor in which fluctuation is hard to detect, but withdrawal of the contained fluid will clear up this point. The presence of multiple cysts, the slow growth of the tumor, the occasional

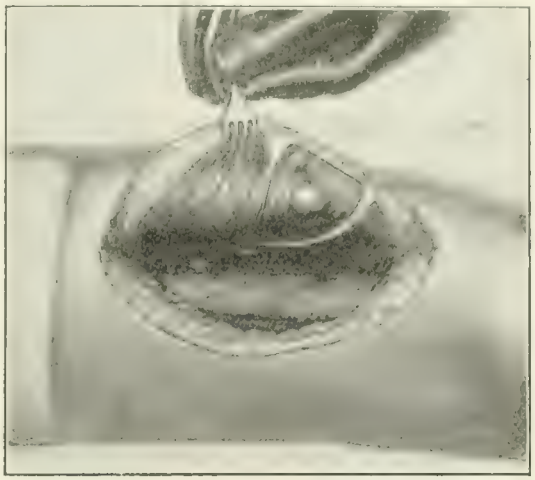

Fig. 1118.—Plastic Resection of the Breast for Cystic Disease. Breast reflected upward. (Warren, Annals of Surgery, June, 1907.)

oozing of a darkish fluid from the nipple, the absence of nipple retraction and skin dimpling, together with the non-existence of glandular infection, are strong points in differentiating it from carcinoma.

Treatment.—The fact that recent investigations have demonstrated the readiness with which cystic formations of the breast, ordinarily considered innocent, may assume carcinomatous features, shows that

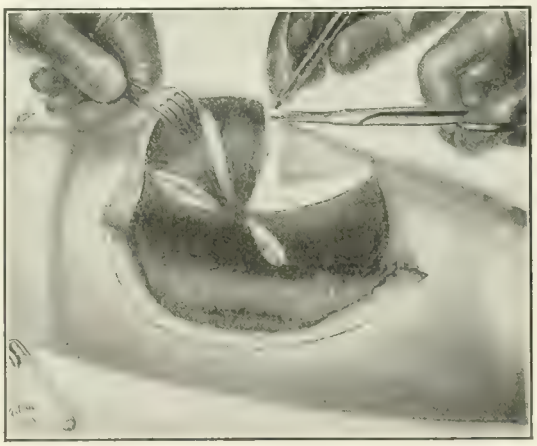

Fig. 1119.—Plastic Resection of the Breast for Cystic Disease. Radiating incisions following removal of large cyst; excision of medium-sized cysts and incision of small ones. (Warren, Annals of Surgery, June, 1907.)

operative intervention should never be limited to puncture and aspiration, or that such a method as forcible massage should be resorted to. The large single cysts should be excised together with a good margin of gland tissue, when the cyst-wall is not thickened and the contained fluid is not bloody. If the cyst is large, or the cyst-wall infiltrated, or

when the breast is generally riddled with cysts, amputation is to be recommended. Abbe and other surgeons have advised simple tapping (and the possible injection of iodine, etc.) in large cysts, but the case of Curtis, where cancer was demonstrated in a smooth-walled cyst with normal surroundings, together with the reported cases of McGraw and others in which

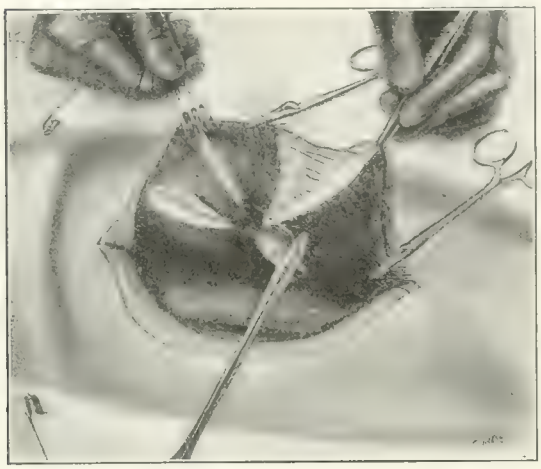

Fig. 1120.—Plastic Resection of a Part of the Breast for Cystic Disease. Method of suturing a V-shaped wound. (Warren, Annals of Surgery, June, 1907.)

aspiration of the cyst was followed by the development of carcinoma, alone offer quite sufficient reason for the abandonment of a procedure that may be potent for evil.

Appreciating that amputation of the entire breast is a formidable operation for the removal of a disease usually benign, J. Collins Warren has adopted a pro-

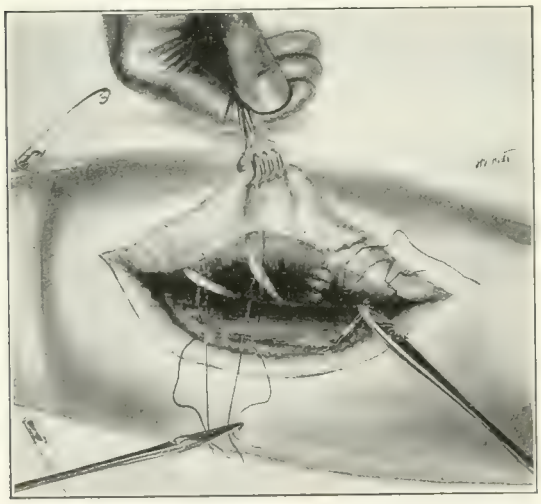

Fig. 1121.—Plastic Resection of the Breast. Adjustment of gland to outer edge of pectoral muscle. Self-closure of radiating incisions. (Warren, Annals of Surgery, June, 1907.)

cedure, modelled after the operation of T. Gaillard Thomas, by which the breast is turned back and the cysts excised as may be required, even to the extent of removal of the entire gland. This he designates, plastic resection of the breast.

Technique of Plastic Resection of the Breast.—The incision is placed at the outer and lower border of the breast (instead of entirely below in the inframammary crease, as in the Thomas incision) and extends in a curved sweep around the organ from the lower end of the outer hemisphere along the axillary border, and should be sufficiently long to freely expose the upper and outer quadrant of the gland. Where conditions require it the incision may extend from one-half to two-thirds of the circumference of the breast. The incision is now deepened to the pectoral fascia and enters into the loose cellular tissue between the mammary gland and the fascia; at the same time the left hand of the surgeon reflects the breast upward and everts its posterior wall through the wound thus made. This affords a full exposure of the under surface of the gland, and the greenish-blue color of the cyst is easily recognized through the mammary fascia. The cyst is now excised by including it within a wedge, or V-shaped cut through the gland substance, with the apex of the V in the central portion just beneath the nipple, and being careful not to open the larger cysts. The remaining segments of the gland are now explored by radiating incisions to disclose the presence of other cysts, and these cuts may vary from two to eight or more as may be deemed advisable. Any questionable area can thus be easily removed and submitted to microscopic examination, which should be made at the time. The V-shaped incision or inci-

Fig. 1122.—Plastic Resection of the Breast for Cystic Disease. Operation completed. (Warren, Annals of Surgery, June, 1907.)

sions are now closed by a double row of buried sutures of chromicized catgut, which should closely approximate the edges, and the radiating exploratory cuts may be either stitched or left to fall together, which generally occurs when the gland is readjusted in position upon the pectoral muscle. The outer edge of the gland is tacked by a stitch or two to the margin of the pectoral muscle, which holds it securely, and the cutaneous wound is closed with silkworm-gut sutures. The puckered appearance of the surface of the breast, due to suturing the wedge incisions, soon disappears as the sutures are absorbed, and in a short while the breast resumes a natural contour.

This method is widely applicable to the removal of benign neoplasms where complete amputation of the breast is not required. It possesses the advantages of affording an ample field for both examination and removal of the growth at the same time; and, moreover, the incision is so situated as to be readily convertible into one for radical amputation of the breast with dissection of the axilla. The resulting scar is almost concealed and often scarcely visible, which is of much consequence to young women who are anxious about cosmetic appearances.

Evolution cyst is a term applied by S. W. Gross to a single cyst met with in women whose breasts are functionally active.

Another form of single cyst is found in women of middle life, and is a retention cyst arising from a *lacteal sinus*. It is a hard, clearly outlined tumor of moderate size, and usually situated in the upper hemisphere. Pressure may cause fluid to exude from the nipple. Excision is the rational surgical procedure.

Hematoma, or extravasated blood into the tissues of the mammary gland, may remain unabsorbed for a long period of time. It may finally become surrounded by an inflammatory wall, forming a pseudo-cyst. If aspiration and pressure fail to relieve, free incision and gauze packing may be resorted to.

Mucoid Cysts.—These cysts originate in the glandular structure, and are so designated on account of the character of their contents, which resemble the mucus-like secretions found in dilated ducts. This varies from a pale yellow, serous-like fluid, to that of a muddy brown, reddish, or greenish hue, viscid and mucoid in appearance, and is composed of granulo-fatty débris, fat globules, hematin crystals, and cholesterine scales, with albumin. The cyst-wall is of a thin fibrous tissue lined by a layer of cubical epithelium. These cysts are usually single, but there may be several of them, and they more commonly occupy the neighborhood of the nipple and areola; and are seen as slow-growing, smooth, rounded tumors, varying in size from a small nut to a large egg. They may be so tense that fluctuation cannot be elicited, and often under pressure fluid may escape from the nipple, which is a sign of diagnostic importance. The growth is not adherent, the nipple is not retracted, and the axillary glands are uninvolved. It is painless and insensitive on pressure. They seldom appear before puberty, and are oftener found in women of early adult and middle life. They are usually perfectly benign unless associated with other tumor formations. Aspiration will usually remove any doubt as to their nature. Enucleation of the cyst should be practised.

Cysts Associated with Papillomatous Ingrowths.—As the name implies these are cysts in which a papillomatous ingrowth or sprout from the cyst-wall takes place. This intracystic growth may be only of minute size or so large as to fill the entire cyst, associated with a bloody fluid. These papillomata are shown, microscopically, to consist of processes of connective tissue surrounded by several layers of a ductal type of proliferating epithelium. The surrounding breast tissue is not infiltrated unless malignant degenerative changes have supervened.

This character of growth is quite similar to the simple or involution cyst, but much rarer, and the most constant clinical symptom is the discharge from the nipple. This discharge may be of small amount or rather profuse, and varies from a clear serous character to blood stained or bloody, which latter is more generally present. The cysts are seated near the nipple, their cystic character can usually be confirmed by palpation; and they may be of an elongated shape extending toward the nipple. They may exist from a few months to a dozen years, and in some instances spontaneous disappearance has been noted, as Ill has shown. Although these tumors are probably classed among the innocent growths, they exhibit a marked tendency to become cancerous. About fifty per cent. of the cases met with at Johns Hopkins Hospital had assumed malignant changes (Finney).

Treatment.—The treatment, naturally, calls for removal of the whole breast; and where there are evidences of induration and infiltration of the adjacent mammary structure, the procedure should comprise the radical operation for carcinoma—clearing out the axilla and ablating the pectoral muscle.

Cancer Cysts.—These cysts are discussed under the head of carcinoma.

Galactocele (Lacteal Cyst).—This is a type of retention cyst, and is a comparatively rare cystic tumor produced by obstruction or obliteration, followed by dilatation, of a milk sinus or duct. Injury inflicted upon the nipple during sucking or otherwise, is a probable cause of the obstruction. Rupture of the wall of the duct may take place with escape of milk into the connective tissue, which becomes thickened and altered to form a pseudo-cyst wall. Practically, the growth invariably develops during the lactation period, but it has been known to a ise independently of pregnancy, that is, months before and long years after, as shown by the cases of Atlee and of Bouchacourt.

The contents of the lacteal cyst vary with the absorption of the fluid elements, and the chemical changes incident to the age or length of time the tumor has existed. At first this is pure milk; later it may be altered to a turbid fluid with colostrum débris; and an older cyst may contain a creamy or oily matter often resembling butter in consistency and appearance. In still others, as absorption goes on, this may

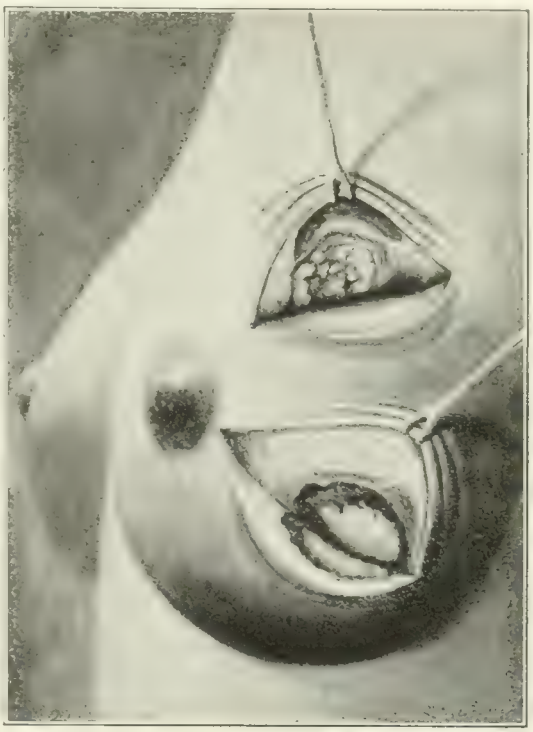

Fig. 1123.—Multiple Galactocele. (Mudd, Am. Practice of Surgery.)

be reduced to a curdy or cheese-like substance. Microscopically the material is found to be almost pure fat. I have seen two such tumors, one as large as an apple, the other somewhat smaller, and filled with a caseous mass almost identical in resemblance to soft cream cheese.

They do not often grow to a great proportion, the average size being about that of an egg, but occasionally cases have been reported where enormous dimensions were attained, as, for example, the patient of Scarpa. The tumor is usually solitary, less frequently multiple; and the consistency will depend upon the contents—the presence of fluid giving fluctuation, whereas if the contents are thick and inspissated there is pitting on pressure, and a doughy or even solid sensation is imparted to the finger. In old cysts the wall may undergo calcareous degeneration. The tumor is usually situated beneath the nipple or the areola,

at the seat of a lacteal sinus. It is mobile, there are no attachments, and it is without pain or inflammatory reaction. If occlusion of the galactophorous duct originates in a lobule, the growth is deeply seated and away from the nipple. When superficial it appears darker under transillumination than the contiguous skin. The growth may be rapid at first, but with the cessation of lactation it may shrink in size, become more solid, and remain apparently unchanged until another lactation supervenes when it again assumes greater dimensions.

The onset is somewhat sudden, and it appears as a small, ovoid, tense, and smooth swelling, unless rupture of the duct has occurred when it becomes irregular or lobulated in outline. Compression of the tumor, if it be in the areola space, may cause a milky fluid to exude from the nipple. When these tumors reach a large size suppuration and ulceration may occur, together with the formation of milk fistulæ, but this is an uncommon complication. It is probable that many of the hard nodules in the breast of young mothers, and usually considered to be lobular mastitis are due to retained milk; and again it is also not improbable that some of the cases of acute mastitis with abscess originate from the same source (Warren).

Some remarkable instances of galactoceles occurring in axillary mammæ have been related by W. Roger Williams.

Diagnosis.—Difficulty in diagnosis is not experienced except in old cases, after long retention of the fluid, and where the cyst contents become semisolid. But the clinical history, namely, the fact that the tumor appeared during lactation, its stationary condition between pregnancies, normal nipple and lymph glands, together with the results of aspiration should enable one to avoid mistakes.

Treatment.—Small lacteal cysts in nursing women may be dissipated by puncture and strapping the breast. Incision with subsequent gauze packing will effect a cure in certain cases. Aspiration followed by injection of tincture of iodine is not to be recommended. In the majority of instances, however, excision and immediate suture, by a plastic resection operation, is the preferable surgical procedure. Where the sac is thickened and indurated, Keen advises amputation of the breast.

Dermoid Cyst.—Dermoid cysts of the anterior aspect of the chest, especially in the upper and midsternal region, have been met with in a fair number of instances; but dermoids of the mammary gland proper are of great rarity. In fact it has been claimed by some writers that no genuine case of such formation in the breast has ever been observed. Roger Williams, however, has collected from the literature four cases, reported by Hermann, Reverdin and Mayor, Albers, and Velpeau, which seem to be of undoubted dermoid character, and which should occupy a legitimate place in this category. The cases are too few to permit the assemblage of any distinctive symptoms, although these seem in no wise different from those of other mammary cystic growths. It is well to note, however, that in two of the four cases (the situation in the others not stated) the cysts were located in the lower hemisphere of the breast; that they were of very slow growth, remaining almost stationary for years; and that the nipple and axillary glands were normal. Ulceration of the skin existed in one case. Dermoid cyst is stated to have been observed in the male breast.

Treatment.—If the cyst is of moderate size the simple enucleation of the tumor is called for, as practised in other cystic growths. This should be done, if possible, without rupturing the cyst, and particular care should be exercised in the dissection to avoid leaving behind the smallest portion of the sac, lest this become the nidus from which repullulation takes place. With large cysts complete removal of the breast is the preferable procedure.

Echinococcus Cyst (Hydatid Cyst).—The scolex of the tænia echinococcus only occasionally finds lodgment in the mammary gland, and, therefore, echinococcus cyst is quite an uncommon affection of this locality. But a sufficiently large number of cases have been observed to necessitate its being reckoned with in considering diseases of the breast. It may occur in the male as well as the female mamma.

Le Conte in 1891 collected and published thirty-three cases of true hydatid disease of the gland, including a case of his own which he regarded as the first one of the kind occurring in America. The cyst ordinarily grows very slowly, is unattended with pain, and in several cases an hydatid colony has been known to exist in the mamma for a period of ten years or longer without causing material discomfort. It may be smooth and rounded, but sometimes is irregular in outline, may develop in any part of the breast except in the nipple and areola, and seldom attains any great dimensions, although cases are on record where it has reached the size of a child's head. They occasionally become inflamed and suppurate, which causes adhesions to adjacent tissues and enlargement of the axillary lymph glands.

Diagnosis.—The great rarity of the disease makes the diagnosis difficult, or even impossible in some instances, before operation or the spontaneous opening of the cyst with extrusion of daughter cysts. When seen at an early stage in young women, it might readily be mistaken for a benign growth; and at a later period if in older women, the firmness of the tumor, its sometimes irregular contour and tendency to implicate the skin, would be strongly suggestive of carcinoma. The fluid contents of the hydatid cyst are non-albuminous, differing in this respect from the fluid of other mammary cysts, and often containing the characteristic hooklets and scolices. Hence aspiration of the sac and a microscopic examination of the withdrawn fluid should clear the diagnosis, but it should be remembered that in only about one-half of the cases are the hooklets to be found.

Treatment.—The treatment should be governed by the size of the cyst, age of the cyst, and character of the cyst-wall. This will vary from simple enucleation by dissection, free incision, and application of iodine with gauze packing of the sac, to partial or complete amputation of the breast.

Tumors of the Breast.—*Classification.*—Tumors of the mammary gland are clinically divided into two primary classes, namely, the *benign* and the *malignant* growths; although such a division cannot be regarded as being without question, since many of the benign neoplasms assume malignancy during some period of their life history. But beyond this, an entirely acceptable and scientific classification of breast tumors still remains to be elaborated. The fact that these tumors are represented by such a variety of types, together with the many and changing terms applied to the same pathological conditions, and the assembling of these morbid findings into different systems, has produced a state of much confusion and disagreement.

This perplexity is the greater in regard to the pathological grouping of the benign tumors of the breast, and the nearest approach to an orderly arrangement of these formations is the one proposed by J. Collins Warren, based upon the suggestion of Ribbert. This division of the benign tumors, as applied to those of homologous structure, will be adopted in the present discussion. However, the prime question and the one of great practical importance alike to the patient and to the surgeon is, Whether the growth is benign and presumably curable, or malignant and probably incurable? But it should be remembered that all mammary tumors are potentially malignant, and that benign neoplasms are subject to malignant degeneration in both the male and female breast.

The male breast is subject to the same diseases and new-growths as are found in the female gland, except those connected with the function of lactation. Neoplasms, however, are decidedly less frequent in the male breast, which is accounted for by its embryonic and rudimentary state together with the absence of physiological glandular activity, especially those changes dependent upon gestation. Various estimates of the relative proportion of tumor-growth in the two sexes have been made, but it may be broadly stated that fully ninety-nine per cent. of all mammary tumors occur in the female mamma and only about one per cent. in the male breast.

I. BENIGN TUMORS.—Histologically considered the benign neoplasms of the breast are structurally composed of tissues indigenous or normal to the mammary gland, as contrasted with the malignant class; and, again, clinically they present characteristics equally distinctive of their type. Thus, the benign tumors occur at a much earlier age, being sometimes encountered in childhood; they are definitely circumscribed and encapsulated, and more frequently multiple; they are for the most part mobile, not adherent to adjacent structures, and the overlying skin and fat are usually unchanged. They are apt to be of slow growth, and as they enlarge they displace but do not infiltrate the surrounding tissues. Their consistency is usually softer, and pain and tenderness are more pronounced than in malignant tumors. Metastases are absent, and the axillary lymph nodes are seldom involved. Discharge from the nipple is another feature suggestive of benignancy, unless it be bloody in character when it is more apt to be associated with a malignant condition.

Benign tumors of the breast are much less frequent than malignant tumors. In an analysis of 5,000 cases of mammary tumors, taken largely from German clinics where the microscopic findings were presumably more likely to be accurate, Rodman found that 16.5 per cent. were benign.

Williams found six benign growths among twenty-five tumors of the male breast; and in Schuchardt's first collection of 295 tumors, 274 were malignant and 21 benign.

When occurring in childhood they are much more frequent in girls than in boys, although the disparity in numbers is not nearly so great as between the sexes in adults.

The rarest of the benign mammary tumors occurring in both the male and female, are those composed of only a single type of tissue, such as fibroma, myxoma, angioma, adenoma, myoma, etc.

Warren's classification is based upon the two separate structures which are so intimately connected with the development of the mammary gland, namely, that peculiar transparent myxomatous connective tissue surrounding the terminal ducts and acini, first mentioned by Billroth, and which is characteristic of the early stages of the young breast; and, secondly, the epithelial elements, which reach their mature development in later life, especially during the changes incident to pregnancy and lactation. Warren shows that these two tissues are so closely associated that a new growth of either one must necessarily share in the essential features of both structures. In other words, that a neoplasm of the periductal fibrous glandular tissue cannot develop in any proportion without implicating to a great or less degree the duct epithelium; and, again, that a tumor arising from the epithelial elements must likewise involve the fibrous structure, unless it be of a true carcinomatous type. Therefore, the term fibroepithelial has been given to this class of tumors as emphasizing the two essential structures of which they are composed. Furthermore, Warren has divided these fibroepithelial growths into two groups, viz., (1) the fibrous, and (2) the epithelial, according to the preponderance of the fibrous or the epithelial elements. This distinction, he states, is sanctioned clinically by the fact that the fibrous group has a distinct tendency to sarcomatous transformation, while the epithelial group evinces a predisposition toward carcinomatous change. The tumors of the fibrous group are marked by the predominance of fibrous tissue, while the epithelium that is present is of small importance; and in the tumors of the epithelial group the existing fibrous tissue is distinctly subordinate to the predominating epithelial element.

(1) THE FIBROUS OR CONNECTIVE TISSUE GROUP of tumors are mixed growths, and from the similarity of the connective tissue of which they are composed to that surrounding the terminal ducts, Warren has designated them periductal tumors, and divides them, according to the character and richness of their cells, into three subgroups, (a) periductal fibroma, (b) periductal myxoma, and (c) periductal sarcoma.

(*a*) *Periductal Fibroma.*—This type of growth has been designated by a variety of names, among the more prominent of which may be mentioned intracanalicular papillary fibroma, intracanalicular myxoma, fibroadenoma, adenofibroma, cystosarcoma, chronic mammary tumor, and so on.

Pathology.—In a recent communication, Greenough and Simmons detail the results of a careful study of a series of twenty-seven cases of periductal fibromata, and from this paper I have liberally drawn in the following section.

The gross appearance of a section of these tumors shows a grayish-white or pink, irregular surface having either pearly translucent spots, or clefts, scattered about over it. The whole growth is frequently divided into lobular masses, and in not a few instances it has a gelatinous appearance due to an edematous condition of the fibrous tissue, which has caused certain authors to classify these tumors as myxomata. The translucent areas above metioned represent the severed ducts and lobules of the mass, and the clefts and minute cysts are often produced by the distortion and choking of these ducts. The cleft-formation may be so pronounced in large tumors as to present the appearance of a large cyst filled with numerous rounded papillary outgrowths of fibrous tissue from its walls, to which type of tumor the term intracanalicular papillary fibroma is often applied.

Microscopically these growths are made up of a fibrous tissue stroma, divided into lobular masses by bands of dense connective tissue, which forms the framework of the tumor and gives support to the lymphatics and blood-vessels, and through which pass ducts with epithelial lining, cysts, and clefts. The whole mass may be likened to one of the racemose gland lobules of the breast. Fibrous tissue is the greatest component of the tumor, and resembles the hyaline connective tissue intimately surrounding the ducts in the immature breast. This tissue is delicate and richly nucleated as compared to ordinary connective tissue, and the nuclei of the cells are more oval and vesicular. It also appears succulent or edematous, caused by a fluid separating its fibers.

The epithelial elements are seen in the epithelial lined ducts, or cysts, or clefts. These vary in number and character in different tumors and even in different portions of the same growth. They originate, undoubtedly, from the ducts of the gland, or from the early embryonic epithelial elements from which the ducts are derived, but apparently they are not continuous with the ducts terminating at the nipple. In may cases the epithelial elements are scanty, and appear as various-sized gland ducts, which have been distorted by the growth of the surrounding periductal fibrous tissue. This produces the slit cysts so distinctive of these growths, and suggested the frequently employed name of intracanalicular papillary fibroma. In other instances the epithelial

structures are in greater quantity, and seem to have grown as rapidly as the fibrous element, producing, instead of distorted clefts, a uniform tissue consisting of numerous small epithelial lined tubules separated by a periductal fibrous tissue stroma. In some cases there is a grape-like arrangement of the smaller lobules, while in others this clustering is absent and the lobules are placed irregularly in the fibrous stroma. Tumors having this last or irregular arrangement have been classified as fibroadenoma or adenofibroma, and to these Rodman has recently given the term pericanalicular in contradistinction to the growths with slits or clefts which are described as intracanalicular. The intracanalicular type is the more common.

The epithelial cells of these several forms vary in type from compressed columnar cells to cuboidal, large and clearly defined cells, or even high columnar cells. Cystic formation occurs in both groups of tumors; in the pericanalicular tumors they are usually small, whereas in the other class they may reach a large size.

Symptoms.—These growths represent the common breast tumors in young, usually unmarried, women between the ages of twenty and thirty years. Warren found that forty-five per cent. occurred in females from ten to twenty years, and fifty per cent. from twenty to thirty years old, and then rapidly diminished with the succeeding decade.

They are also the most frequent type of benign tumor encountered in the male breast, which do not differ in any respect from those of the female mamma. Woodyatt divides these growths in the male into two forms, the circumscribed variety occurring in young men and possessing all the microscopic characters of fibroepithelial tumors in the young female breast; and the diffuse form, usually called fibroadenoma, which are met with at any age and are frequently produced by traumatism. Adolescent mastitis is also stated to be a positive causative factor. Denenholtz mentions a case of bilateral tumors in a boy fifteen years of age.

These growths are frequently multiple but oftener single, and occur equally on the two sides and sometimes in both breasts; they are found in any portion of the gland, but with an evident preference for the upper half of the organ and particularly the outer quadrant.

Billroth has noted the interesting fact that these tumors do not interfere with the normal gland development, but that the tumor undergoes lactation hypertrophy along with the breast, and the secretion of milk proceeds naturally.

These tumors are distinctly encapsulated, and vary in size from a hazelnut to a large apple, or may even attain an enormous size. The contour is usually of an irregularly round and lobulated, or bossed, outline, and the large growths are of a hard, firm, or fibrous consistency, except in the presence of cystic degeneration when softening of the mass is discernible. The small tumors are elastic in feel and generally rounded, and may be mistaken for cysts. When of early growth they are freely movable beneath the surface and show no tendency to implicate the skin or subcutaneous tissues, except in very large tumors where an inflammatory process may cause adhesions. Discharge from the nipple is very infrequent. These formations are of slow growth and long duration, although it occasionally happens that a sudden activity in growth sets in after a long period of quiescence. Ordinarily they are without pain, except at the catamenia when they may become decidedly painful and sensitive.

Diagnosis.—The characteristic features of these tumors are those distinctive of benign tumors in general, and have already been dwelt upon, but may be summarized as follows: They are oftener single than multiple; occur in young women; grow slowly; are painless; round and lobular but with clearly outlined margin; usually hard and resistant, but often elastic in consistency; mobile in the early stages, and seldom adherent to adjacent structures; there is no discharge from the nipple; and the axillary lymph nodes are not affected.

Treatment.—These tumors should be removed. Bloodgood, with some other surgeons, advise against operation when they occupy both breasts, are multiple, and of small size, since they may ultimately disappear. A short radial incision is usually sufficient for their removal and leaves a scarcely visible scar. In those cases with troublesome symptoms, and particularly where the tumor assumes sudden activity in growth—suggestive of possible malignant degeneration—the whole breast should be removed together with the muscles, although it is not necessary to invade the axilla.

(*b*) *Periductal Myxoma.*—These tumors are quite similar in structures to the preceding type or fibroma, being composed of a myxomatous fibrous tissue which

Fig. 1124.—Periductal Myxosarcoma (Low Power). Portion of tumor showing cell-rich stroma of sarcomatous periductal tissue, gland ducts, and cysts and encapsulation. (Greenough and Simmons, Annals of Surgery, October, 1911.)

is succulent, or, rather, edematous; and the principal clinical difference between them is that the myxomata attain a larger size, and are found in the breasts of both single and married women (oftener in the latter) of middle age, rather than in young women. They are usually hard, firm, growths, although the greater number of them contain cyst-cavities; they are disposed to necrosis; and the axillary lymph nodes are not infrequently enlarged. There is no discharge from the nipple.

(*c*) *Periductal Sarcoma.*—This third subgroup of periductal mammary tumors is characterized by a stroma rich in cells combined with gland ducts. Clinically, it is noted that these growths are commonly encountered in married women of medium age; that they grow rapidly; are usually large; may even reach enormous dimensions, and often the whole breast is involved in the formation. They are encapsulated, hard, and irregularly lobulated, but softened

areas from degenerative changes are not infrequent; sometimes they contain cysts; the overlying skin is stretched, with large veins coursing over it, but not adherent, although ulceration may occur; and the axillary glands are only rarely involved. There is no fluid exudation from the nipple. Pain is not a positive symptom, the only discomfort experienced being that attributable to the size and weight of the organ.

Greenough and Simmons believe that the distinction between the periductal myxoma and the periductal sacroma is but an arbitrary division, and prefer to classify them under the one term of "periductal myxosarcoma." This merging of the two subgroups into a single one seems to possess certain advantages, and hence will be adopted in the further description of the subject.

This class of myxosarcomata have also an extensive and varied nomenclature, being known under the captions of adenosarcoma, fibrosarcoma, fibromyxosarcoma, cysticsarcoma, and many other terms. This variety of tumor is relatively rare, but, at the same time, it is the commoner form of mammary sarcoma.

Pathology.—A section shows distinct encapsulation, with a lobulated surface of a semitranslucent gray color, and with cysts or clefts interspersed throughout. The cysts range in size from just visible bodies to that of a large orange, contain a brownish fluid, and sometimes cystic papillary outgrowths exist.

The microscopic findings vary. The connective-tissue stroma is divided into lobules by bands of fibrous tissue, and is more or less rich in cells. Interspersed throughout the stroma are clefts and cysts, and ducts lined with epithelium. The connective tissue is different in different portions of the growth—it may be the loose periductal fibrous tissue, the myxomatous tissue composed of delicate processes and stellate cells, or the more closely packed fibrosarcomatous tissue. The fact that tissues made up of these several types of cells are often in juxtaposition, frequently makes the separation of the periductal myxoma from the periductal sarcoma a matter of impossibility. In the large tumors hyaline degeneration is common.

The epithelial elements are identical in every particular with the epithelial structures of the periductal fibroma. The resemblance, both microscopical and clinical, between the two groups of neoplasms is so very marked that the conclusion is forced upon the observer "that the myxosarcoma is a periductal fibroma, the fibrous tissue of which has more or less taken on the change in characteristics (anaplasia) which marks the advance from benign to malignant tumor-growth—a change which, whether correctly or not, is often spoken of as degeneration."

Diagnosis.—The clinical features of the periductal myxosarcoma may be thus briefly stated: They are of rather rapid growth, and of large size; are found in middle-aged women; are encapsulated and lobulated; they are somewhat prone to cystic formation and to degeneration; the skin is not adherent unless ulceration occurs; the axillary nodes may be enlarged; there is no discharge from the nipple; and they are usually devoid of pain.

Treatment.—As a rule, the myxomata only require local removal, unless associated with symptoms of degenerative change when amputation of the entire breast should be practised. With the sarcomata, however, amputation of the gland is always the required procedure; and in advanced cases, or where growth is rapid, the dissection should include both the muscles and the axillary space, which usually carries with it a favorable prognosis.

(2) The epithelial group, or cystadenoma, is subdivided into (a) fibrocystadenoma, and (b) papillary cystadenoma.

(a) *Fibrocystadenoma.*—This type of the fibro-epithelial class of tumors is principally found in young, unmarried women, and the tumors are usually of slow growth and painless. They may be seated in any portion of the breast, and even in both glands. They are lobulated, of a hard, firm consistency, mobile, and vary from the size of a large nut to that of an apple; the axillary nodes are not hyperplastic. The growth has a distinct capsule, the tumor structure is lobular, and contains various-sized cysts with epithelium-covered outgrowths of connective tissue. The pathological process involves the gland ducts rather than the acini, and evidently represents the initial step toward malignant metamorphosis.

(*b*) *Papillary Cystadenoma.*—This second variety of the epithelial group of neoplasms is rather uncommon. These tumors are single or multiple, they grow slowly, are of long duration, and occur more commonly in married women of mature middle life, but they have been found at all ages, and seem to be independent of lactation or trauma. They are hard, firm, usually small growths, although occasionally soft and indistinctly fluctuant; and may assume a large size. Ordinarily the skin, as well as the axillary lymph glands, remains unimplicated; and they are the source of but little pain or other disturbance. The location of preference in the breast seems to be in the larger ducts just beneath the nipple. A bloody discharge from the nipple is frequent and considered a symptom of pathognomonic importance. Greenough and Simmons report them associated with a low grade of cancer (adenocarcinoma) in fifteen per cent. of a series of twenty cases.

Fig. 1125.—Fibrocystadenoma (Low Power). Showing large number of gland ducts and cysts in proportion to stroma, and active proliferation of epithelium. (Greenough and Simmons, Annals of Surgery, October, 1911.)

On section of the growth there is seen a cyst cavity filled with a bloody fluid, and the walls covered with papillary outgrowths of connective tissue thickly covered with epithelium derived from the ducts—the acinal epithelial cells not usually being in evidence.

The fibroepithelial group of mammary tumors have received the various names of cystadenoma, cystadenoma proliferens, adenoma, papillary cystadenoma, tubular adenoma, polycystadenoma, duct papilloma, villous papilloma, cystic fibroma, and many others. They are distinctly epithelial in type, but at the same time are benign, except in a late stage when they evince decided tendency toward cancerous transformation. They differ from the periductal fibromata only in the relation of their elements, their characteristic or diagnostic feature consisting in the great hyperplasia of the epithelial structures.

These tumors also exist in the male breast, although they are less common than the fibrous or connective-tissue group (fibroadenoma), and present identical characteristics with similar growths in the female mamma. They are usually seen between the ages of forty-five and sixty years, although they are often met with in youth and early manhood.

Pathology.—In general appearance, these tumors are enveloped in a dense, fibrous capsule, their consistency is firm and hard, or firm and elastic, and are irregularly rounded or lobulated in shape.

A section of the growth presents an appearance similar to the periductal fibromata, being firm and fibrous, and of a dull white, sometimes translucent color. The ducts and acini are observed on the surface as many soft, glistening spots, which exist in greater numbers than in the fibromata. Sometimes the cut surface is covered with slits, in other words, being of the intracanalicular type. The small cysts are filled with either a serous-like fluid or the contents may be rather thick or pultaceous in character.

As just remarked, the chief point of difference between these tumors and the periductal fibromata lies in their relatively large epithelial composition as compared to the fibrous tissue they contain, together with the active growth of the former element. The tumor tissue has a lobular arrangement, especially so in the larger growths. Like the periductal fibroma,

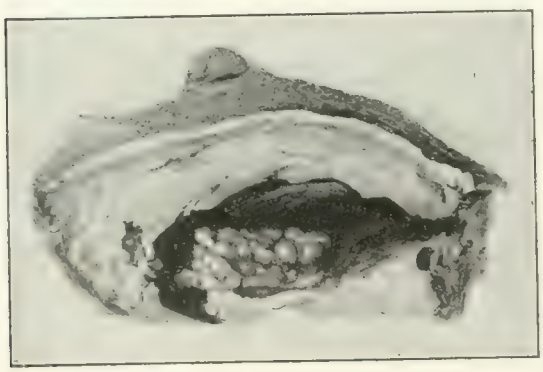

Fig. 1126.—Papillary Cystadenoma; "Villous Papilloma." Gross appearances. (Massachusetts General Hospital, R. B. Greenough.)

the stroma consists of a loose, cellular fibrous tissue, derived from the periductal connective tissue, and without round cell infiltration. Two separate types are recognized, as in the periductal tumors, the intracanalicular and the pericanalicular. The pericanalicular type seems to be the more common, and the suggestion has been offered that the pericanalicular type of periductal fibromata is that from which the fibrocystadenoma is chiefly derived. Epithelial-lined cysts are more frequent than in the fibroma; many glands are lined with only one layer of epithelium, and in others there is a heaped-up arrangement forming papillary growths projecting into the lumen and which may even entirely choke the lumen. There may be an adenomatous arrangement of the cells—an extreme epithelial proliferation—similar to that in cases of involution, which have a disposition to become cancerous.

Diagnosis.—From a clinical standpoint these tumors are inseparable from the periductal fibromata. All of the symptoms and physical conditions are practically identical, and, unless a large cyst is present, yielding distinct fluctuation, the diagnosis must be conjectural until microscopic aid is invoked.

Treatment.—The possibility of the transition of these tumors into carcinoma must ever be borne in

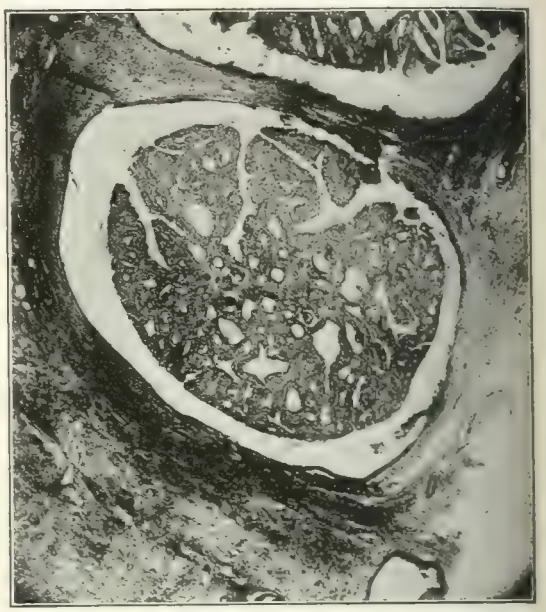

Fig. 1127.—Papillary Cystadenoma. Microscopic appearances. (Massachusetts General Hospital, R. B. Greenough.)

mind, and a proper histological study is necessary to determine the extent to which surgical intervention should be carried. In the fibrocystadenomata, ordinarily it is sufficient to excise them by a small incision, or by the plastic resection method; and the same simple local removal is applicable to the small papillary cystadenomata. But in either instance, particularly the last, when the neoplasm has existed a long time, is of large dimensions, with axillary gland involvement, the modern radical breast amputation should be performed. Non-recurrence may usually be promised after thorough operation.

Mixed Tumors of the Breast.—There are occasionally encountered certain rare forms of mammary tumor containing structures foreign to the normal breast, and whose characteristics bear a close resemblance to the mixed growths of the parotid gland. The histological composition of these tumors is very irregular, and they probably spring from embryonic intraglandular inclusions. They are always encapsulated, pursue a benign course, and may occur at any period of life from adolescence to advanced age. Microscopic examination is invariably required for a positive diagnosis (Finney).

In all cases when the neoplasm assumes rapid growth and other symptoms of activity, amputation of the breast should be resorted to, although it is seldom necessary to excise the muscles or empty the axilla.

Lipoma (Fatty Tumor). True intramammary lipoma is one of the rarest of breast tumors. W. Roger Williams, in 1894, was able to find only three

published examples (out of 2,397 cases of consecutive neoplasms of the female breast analyzed), which were the cases of Koehler, Bégouin, and Sir Astley Cooper. This is a fact worthy of comment when we consider the excess of adipose tissue surrounding the mammary structure and the increased fat deposit in the interstitial tissue of the gland during involution. Occasionally an enormous overgrowth takes place in the paramammary fat or fatty capsule of the gland associated with senile changes and certain circulatory disturbances, producing the so-called *capsular lipoma or mammary lipomatosis*, which should be distinguished from genuine lipoma.

Comparatively frequent, however, are the circumscribed mammary lipomata, which arise from the paramammary or the subcutaneous adipose tissue over the front of the breast; they seldom attain a large size, and are usually found in women between twenty and thirty years of age.

Retromammary lipomata are also occasionally encountered. They usually originate in the fascia of the pectoralis major muscle and often grow to an enormous size. Examples of such retromammary growths are seen in the frequently mentioned cases of Billroth, Sir Astley Cooper, and others. Billroth's case was of immense proportions, displacing and pushing forward the flattened gland before it; and the tumor in Cooper's case weighed fourteen pounds.

A number of cases of true lipomata of the male breast are recorded in literature. They do not differ from those occurring in the female organ, and are commonly found in men of middle life. They are ordinarily of moderate size and slow growth, but may increase rapidly and reach a large size. A case recorded by Masse was of congenital origin and grew as large as an orange in the short space of nine months; and Queirel mentions a fatty tumor that in fifteen months had grown to the dimensions of a child's head.

Diagnosis.—The diagnosis should not offer material difficulties. The subcutaneous type possesses the same characteristics of like growths elsewhere, namely, a soft and elastic consistency, semifluctuant in feel, loose attachments to adjacent structures, and distinct lobulation. It may be mistaken for a mammary cyst, as in the instances mentioned by Velpeau and others.

In the intramammary and retromammary forms, the differentiation may be much less easy. These will be probably oftener confounded with hypertrophy of the breast, as was done in Billroth's case, and followed by amputation of the breast.

Extirpation is the proper surgical procedure. In small and superficial tumors this is quickly done by a short radial incision directly over the mass; but in larger growths and those of retromammary origin, plastic resection of the breast should be the method of election.

Vascular Tumors (Erectile Tumors, Angiomata, Nevi).—Vascular or erectile tumors of the breast are relatively infrequent, and when seen are usually situated in the superficial structures. A fair number of cases are on record. Jopson, Speese, and White have recently discussed this subject in an interesting article, basing their study largely on the data collected by Malapert and Morichant.

These formations are commonly congenital or first appear in infancy, and they have been observed in the breasts of both sexes.

The *cutaneous or nevoid type* are generally of small size, and more often located on or close to the nipple. They present no features differing from nevi found in other localities, and are for the most part of little importance.

The *subcutaneous class* is represented by small, circumscribed, nodular formations in the cellular tissues, and without involvement of the integumentary system. They are apt to cause glandular atrophy by pressure.

The *intramammary* or *glandular types* constitute the true angiomata of the breast. Their precise origin in some cases is difficult to determine. Rarely they are encapsulated, and occasionally they may be diffuse, as Bojardi's case exemplifies. If situated in the nipple area the glandular elements may suffer through pressure atrophy, although the ducts usually resist this process. They occur more often at birth or during the early months or first years of life; they seem to affect both sexes equally; but show a predilection for the right mamma, and in one case bilateral tumors existed (Bittner's case). They may be present for years before being discovered. Pain may or may not be complained of, and there may be but few symptoms besides enlargement of a few superficial veins. If the skin is invaded and ulcerates, active bleeding may follow. In the greater number of instances the tumor is smooth, but sometimes it is irregular or nodular, and when cystic degeneration occurs fluctuation is perceived.

Diagnosis.—The nevoid or skin angiomata are generally recognizable at a glance, and the subcutaneous forms should scarcely offer difficulties in diagnosis, but the deep-seated intraglandular types may be accompanied by marked obscurities. In the majority of instances, however, the sponge-like compressibility of the growth and its prompt return to its original size upon relaxation of the pressure, are pathognomonic symptoms. Pulsatile movement may sometimes be felt.

Treatment.—The simple nevoid growths may be excised; destroyed by the galvanocautery, or by the application of liquid air, or by carbon dioxide snow, the latter agent having recently been employed with gratifying success. The old strangulation method is practically obsolete.

In the larger subcutaneous and intraglandular growths, excision is the most satisfactory surgical measure, but, unless care be exercised in the dissection not to invade the vascular structure with the knife, the operation will be attended by serious hemorrhage. Where the entire gland is involved, amputation of the breast should be performed. In extensive cases, particularly large venous angiomata and the arterial or cirsoid forms, trial should be made of Wyeth's boiling-water injection forced deeply into the growth. This brings about consolidation of the structure, shrinkage follows, and a cure is effected without deformity.

Echondroma; Osteoma.—Both of these formations have been mentioned as existing in the mammary gland, male as well as female, but they are to be regarded as of extremely rare occurrence, and some authorities even deny their existence. Astley Cooper describes a tumor of the breast largely composed of cartilage. Billroth states that a great variety of cartilage is found in the mammary structure of bitches, and which exhibits changes having a tendency to the formation of both myxomatous and osseous tissues. Cartilaginous and calcified placques are at times seen in carcinomas, sarcomas, and old adenofibromas, and also in the walls of ancient cysts. Thayer chronicles an interesting case of calcification of the walls of a breast abscess, following the administration of massive doses of calcium lactate and the submammary injection of 500 c.c. of a one-per-cent. solution of calcium chloride, during an attack of typhoid fever. The abscess was opened and packed with iodoform gauze, and he believed that the deposition of calcium salts resulted from the iodine contained in the iodoform combining with the large quantity of lime in the tissues.

Neuroma.—True neuroma probably never occurs in the mammary gland. The little growths of the breast which have been spoken of as neuromata are

evidently identical with those small and painful fibrous formations that sometimes exist around the ends of the subcutaneous nerve filaments in the extremities. They are rare in the breast and are entirely benign. When present they are very tender to the touch, and are quite often the seat of severe neuralgic pains. Their small size may prevent detection.

Roger Williams refers to two cases of *amyelinic neuromata* recorded by Tripier.

Excision of the tumor should be done.

II. MALIGNANT TUMORS.—A malignant tumor is one that is composed of tissue elements exotic to, that is to say, histologically different from, the structure in which it grows, and possesses certain clinical and structural characteristics which distinguish it from the non-malignant or benign class of growths. The two most characteristic features of a malignant tumor are the disposition to recur *in loco* and to renew or reproduce itself in other parts of the body distant from the original tumor. It further differs from a benign neoplasm in being of more rapid growth, and this varies with the character and proportion of the cellular elements composing it. However, the more rapid increase in and the softer and more vascular the tumor, the greater is the tendency to metastasis, which, from a clinical view-point, is usually accepted as indicating the relative degree of malignancy. Another accompaniment of the malignant tumor is a systemic toxemia, as observed in the cachexia and exhaustion generally attendant upon advanced stages of the disease.

The histological differentiation has already been dwelt upon, but will be discussed at greater length as we proceed with this section.

The two distinctively malignant diseases are cancer or carcinoma, and sarcoma.

Carcinoma (Cancer).—Carcinoma of the mamma is a new-growth composed of atypical epithelial cells, which in the majority of cases are derived from the epithelium lining the acini and the ducts of the normal gland and paramammary tissue.

It seems to be unquestionable that the disease is locally confined in its incipiency, but at what time or stage the localizing barrier ceases to exist cannot be answered. Consequently, carcinoma should be always regarded as having passed to the stage of dissemination, that is, capable of direct extension and transmission to remote regions of the organism by the avenue of the lymphatics, and also possibly the blood-vessels, no matter how early it is seen or how small the size of the growth may be.

The exact method by which dissemination of cancer is accomplished is undetermined, but it is generally agreed that the lymphatic system constitutes the chief medium through which diffusion takes place. The principal theory is, that spreading is effected by cancer cells conveyed by the lymph stream, and the manner of such extension together with the many variations and irregularities in the metastasis of cancer, will be more clearly comprehended by a glimpse at the minute arrangement of the lymphatics. It has been shown that definite areas or spaces are drained by definite sets of lymph-vessels which lead direct to certain lymph nodes in one direction, and in the other direction, or the periphery of the space, anastomose by means of a system of delicate radicles with similar fine capillary vessels of other proximate areas (Oelsner). Thus it is seen that occlusion of the outgoing or efferent channel of a given space will be followed by the lymph reflowing to and escaping, by compensatory dilatation, through the minute peripheral vessels communicating with the nearest adjoining space, and thus continue on by way of the non-occluded efferent vessel of this other space to a central destination. This would cause a backward flow of the lymph collected from one of these areas, thereby meeting with a double filter, as it were, one for each end of the efferent channel, namely, the lymphatic gland on the one side and the peripheral plexus of vessels on the other side. Hence cancer cells floating as emboli in the lymph current are intercepted by either the proximal gland filter or farther on by the other or distal line of obstructions. The hypothesis of the blood-vessel transmission of cancer is not altogether tenable, and, if such really occurs, it is only in the most advanced cases when the blood has possibly lost certain definite qualities. Moreover this belief has received a rude shock by Goldman and Schmidt who have demonstrated that when cancer cells gain entrance into the blood current they produce thrombosis, and are destroyed or rendered harmless during the organization of the clot.

The idea that carcinomatous tumors increase by a process of progressive invasion of the adjacent tissues has been offered, and especially by Stiles, Heidenhain, Rotter, and others. Recently Mr. Handley, of London, has developed this conception of dissemination of cancer into an interesting theory which he designates "permeation." He maintains that the disease permeates the tissues in a circle—a centrifugal extension—with the original tumor as a center, by an actual growth of cancer cells. This extension progresses continuously along the path of the ducts and delicate radicles of the lymphatic plexuses and irrespective of the direction of the lymph stream. In this way the tissues are invaded by an increasing zone of disease radiating in all directions. He likens a mammary carcinoma to a biconvex lens, the central thicker portion representing the original cancer focus with the depth of disease gradually decreasing toward the thinner circumference. The rim or edge of the circle is often some distance beyond the limits of the glandular tissue, and is composed of the cancer-charged lymphatics forming the fascial lymph plexus, and which, of course, lie entirely in the plane of the fascia. Handley and other observers believe that this permeation first advances in the plane of the deep fascia, and that infiltration of the skin, the muscles underlying the deep fascia, and the nearby viscera, is a secondary invasion by means of those lymphatic ducts running perpendicularly to this primary fascial plane. This comprehension of the disease, as advancing primarily along the fascial planes, has an important surgical and pathological bearing.

Carcinoma is the commonest of all mammary tumors, and next to the uterus and the stomach the female breast is its most frequent seat. It is variously estimated as being in the proportion of between seventy and eighty-two per cent. of all breast tumors. Billroth found only eighteen per cent. of non-malignant growths in 440 neoplasms of the breast, and McConnell points out that the United States Census indicates that, in the year 1900, there were 3,500 deaths from carcinoma of the breast. Andrews has shown in a series of 7,881 cases of cancer that the breast was involved in 1,232 instances, and, next to the uterus and the stomach, he places the mammary gland as the third most frequently affected region of the body. The statistics of Williams give the breast even a higher rating—40.3 per cent. of all cancers as against 34 per cent. in the uterus.

Carcinoma is also the most common neoplasm of the male breast, being slightly more frequent than all other growths combined. Williams encountered sixteen cases of carcinoma in twenty-five tumors of the male mamma.

Etiology.—The etiology of cancer is unknown. Thus far the laboratory, with all of its marvelous revelations in the science of medicine, has signally failed in the untiring efforts made to disclose this hidden secret of one of the most feared and fatal diseases of mankind. Our knowledge, therefore, of the cause of carcinoma consists only in what intelligent clinical observation has brought to light—

those conditions that have been shown to be intimately connected with the development of the disease.

(*a*) Among these factors *racial* individualities appear to have some effect upon the origin of carcinoma. The affection has long been regarded as rare among the black races, and decidedly more common in temperate than in tropical climates, besides being known to be more prevalent in certain localities of Europe and the United States. Dennis and Warren, both with wide experience in the disease, have noted only a few instances in the negro race. But more recently Rodman has pointed out that carcinoma is relatively as common in the black as in the white race, and quotes from the eleventh United States Census as showing that the death rate from cancer among the white population was 4.27 per cent., and 4.19 per cent. in the colored race, or practically an equal mortality. The Census also shows that it is found twice as often among the foreign born as among the native whites of the United States. Carcinoma has been stated to be rare in India, but Roger Williams quotes Cantlie as saying that it is frequent among the Chinese, and that in a series of one hundred and fourteen cases of cancer thirty-eight were affected with the mammary form. Kerr in one year's hospital work in Canton performed thirty operations for malignant disease, and of these eleven were for cancer of the breast.

(*b*) *Heredity* is undoubtedly an etiological factor to be reckoned with, although there is not perfect unanimity on this point among writers. That there exists a very evident susceptibility to cancer in certain families is well established. S. W. Gross found that heredity (in a direct line of descent) played a decisive part in only 4.72 per cent. of his statistics; and Roger Williams in 138 cases traced a family cancer history in 24.2 per cent. Finney states that it has been reported to vary from three to thirty-three per cent., but he thinks the evidence adduced is insufficient to substantiate the heredity claim, and in line with this opinion quotes Jennings who found a family history of cancer in one out of nine cases where the mammary growth was cancer, and in one out of seven cases where it was benign.

The positive effect of heredity in the causation of carcinoma of the male breast is also claimed by a number of authors. This influence is stated to extend to both benign and malignant mammary growths.

(*c*) *Age* is known to exert a definite influence in the predisposition to cancer. Prior to the stage of puberty the mammary gland enjoys almost complete immunity to carcinomatous invasion, whereas it stands preeminent as the disease of the senile breast. After puberty it is still rare in the young breast until the third decade of life is reached, when it gradually increases in frequency to between forty and sixty years, the so-called cancer age, when it attains its highest rate. Rodman gives the age percentage as follows: Between the ages of twenty and thirty years, 11 per cent.; thirty to forty years, 12.5 per cent.; forty to fifty years, 27 per cent.; fifty to sixty years, 28 per cent. Briefly, the period of greatest cancer activity in the mammary gland is between forty-five and fifty-one years, with an average of about fifty years; and it then steadily declines in frequency until the age of eighty years, after which it practically does not develop. In other words, cancer is emphatically a disease of the retrograding gland.

It occurs as frequently in one breast as in the other, but shows a positive predilection for the upper hemisphere, and especially for the upper and outer quadrant—a situation in near proximity to the axilla. The central areola region is the next of preference; and occasionally it develops in an accessory mammary gland and not connected with the gland proper. The same preference is found in the male breast.

The age at which cancer develops in the male breast is much later than that observed in women, varying from fifty to seventy years with an average of about sixty years. It may occur, however, at an early age, instances of such neoplasms being reported at twelve years, twenty years, and twenty-two years, by Williams, Moore, and Coley, respectively. Lunn has reported a man with mammary cancer at ninety-one years, and this is referred to as the oldest recorded case.

(*d*) *Sex* is most pronounced in its relation to mammary carcinoma, and it is generally reckoned that only one in one hundred of the cases occur in the male breast. Billroth places the percentage as high as 2.82; but Warfield states that in a series of 307 cases of mammary cancer at the Johns Hopkins Hospital, only three were in the male; Keyser found thirteen males in 1,460 cases; Sick mentions only two males in 616 cases; Farentino found only one male in 228 cases; and Mumford had one male in 72 cases.

(*e*) *The sexual* state bears a distinct relationship to mammary cancer. It is estimated that only about twenty-five to twenty-seven per cent. of the cases are seen before the climacteric. It is much commoner in married than in single women, and in women who have borne children than in those who are sterile, and also more frequent in multiparæ. Further figures indicate that from fifty to eighty per cent. occur in married women, of whom eighty to ninety per cent. have borne children and seventy to ninety-five per cent. have suckled them (Finney).

(*f*) It is uncertain what predisposing relationship *traumatism* bears to the development of carcinoma of the breast. The trauma of continued or recurrent mild irritations would seem to be of more significant causal effect than that resulting from a single blow or any one positive injury. The statistics on this point gathered by various investigators show a wide difference in percentage—ranging anywhere from three to fifty per cent., with an average of thirteen to fourteen per cent.—and besides many of the data on which these are based are not without reproach. The cases with a history of incidental injury, or when received at a very remote date before the appearance of the tumor, manifestly should not be included with those in which direct traumatism is noted, and unless these were separated and properly classed any deductions drawn from them must be valueless. However, there are authentic cases on record that have developed carcinoma of the breast almost immediately after an injury was inflicted, and clearly in consequence of the traumatism. And it is readily conceived how a blow or other traumatism delivered upon the breast may arouse a slumbering predisposition to cancer, especially when such an injury is received during the time of retrograde changes in the mamma, a period when the gland is recognized as being the most vulnerable to malignant disease. In addition there is a peculiarly prevalent belief in the lay mind the world over that cancer invariably results from blows or bruises, which should not be wholly disregarded. On the other hand, it should be noted that in the large majority of instances no history of antecedent traumatism is obtainable; and in Gilliam's statistics of traumatic cases in only one-fourth of one per cent. did the disease spring from the scar left after the injury. Therefore as the matter stands the case is not proven, and the largely prevailing opinion among surgeons is that the injury directs attention to an already existing tumor, rather than holding any etiological relationship with the disease.

It would seem that traumatism holds a more definite position as a predisposing factor in cancer of the male breast than it does in the female. In a collection of 406 cases Schuchardt found a history of traumatism in twenty-five of them, and Warfield mentions that such was present in eight of a group of thirty-seven cases. Rodman is emphatic in his statement that traumatism is of much greater importance

as an etiological factor in mammary carcinoma in the male than in the female. Not a few instances are recorded where carcinoma has developed in a nodule remaining after the absorption of a hematoma, or in the scar, following traumatism, among which may be noted the cases of Deitrich, Moore, and Schuchardt. Occupation pressure, as exerted by the constant use of certain tools which impinged against the breast, has been known to be followed by carcinoma of the gland. Even the chronic irritation resulting from the friction of clothing has been suggested as a predisposing cause. But, as just stated, the position of traumatism in the etiology of carcinoma is far from being determined.

(*g*) *Mastitis* in its several forms, together with other inflammatory lesions of the breast, is justly credited with a direct influence in the causation of mammary cancer.

The frequency of suppurative lactation mastitis, both acute and chronic, which occurs during the puerperium (six per cent.) furnishes, as would be expected, the basis for a large percentage of carcinoma of the breast. It has been demonstrated that in from twenty to twenty-two per cent. of all cases there is a history of puerperal mastitis. Dennis asserts that mastitis from all causes is the starting-point of thirty per cent. of cancer cases; but this conclusion is materially vitiated from having included traumatic inflammations among the cases. Rosenstein states that mastitis had involved the cancerous side in only eight per cent. of his cases; but as Finney remarks, the relative frequency would be much greater if due allowance had been made for those women with carcinoma mammæ who have never lactated, since they constitute no inconsiderable proportion of cancer cases. Carcinoma has frequently arisen from cicatrices remaining after acute mastitis.

It is the chronic forms of mastitis with persistent local indurations which offer conditions especially conducive to malignant metamorphosis.

Involution mastitis must be regarded as a positive causative factor in mammary cancer. Bloodgood, Greenough, and Hartwell, together with several other observers have sufficiently attested to this relationship.

Adolescent mastitis has been noted as a predisposing cause in the male breast.

(*h*) The *transition from a benign growth* of the breast to a state of malignancy has been abundantly proven by both clinical and pathological testimony. In repeated instances tumors of the mammary gland, of long duration and to all appearances entirely innocent, have without warning or assignable reason put on a malignant garb; and this, too, to the chagrin of the surgeon who may have assured the patient that the formation was benign in character and inconsequential. Such cases are not so infrequent as may be supposed, and should add to the caution in expressing an opinion in all early breast tumors.

In the section on the benign neoplasms of the mammary gland this tendency to assume malignant features was emphasized, and it was then shown that pathological investigation had amply demonstrated this fact. It was also indicated that this disposition varied with the cellular constituents of the growth, and that the cancer predisposition increased with the degree of epithelial proliferation, and diminished with the degree of connective-tissue predominance. However, it was also explained that even in those neoplasms composed essentially of connective tissue, there was always present a certain proportion of epithelial elements which were capable of abnormal changes and of setting up carcinomatous degeneration in the growth. The weakness of the connective tissue elements to sarcomatous transformation is of course understood. Therefore it is in the epithelial group of the fibroepithelial tumors that cancer metamorphosis is more often exhibited, and especially those of the papillary-cystadenoma type in which the percentage of malignant change rises to fully fifty.

Tumors of the male breast may undergo malignant degenerative changes identical with those in women. Owens and Eisendrath report carcinomatous formations in a fibroadenoma.

Pathology, Varieties, and Classification.—Carcinoma of the breast is divided into two general classes, namely, the primary and the secondary.

The primary class, which is by far the most common, is usually divided into: 1. Glandular carcinoma; 2. adenocarcinoma; 3. colloid carcinoma; 4. Paget's disease (malignant papillary dermatitis); and, more recently, 5. cancer cysts.

1. Glandular carcinoma is sometimes also divided into three varieties, according to the proportion of connective tissue present in the growth, as (*a*) medullary carcinoma; (*b*) carcinoma simplex; and (*c*) scirrhus carcinoma.

(*a*) *Medullary Carcinoma.*—This form is known as encephaloid or soft cancer, and is characterized histologically by the large proportion of epithelial elements and the relatively small amount of stroma or connective tissue that it contains. It appears at a much earlier period of life than does the scirrhus variety. It is also rare, representing from two to four per cent. of these tumors, and is generally classed among the most malignant neoplasms of the breast, although Finney states that such is not the experience in the Johns Hopkins clinic. The epithelial cells are of a glandular form, and the alveoli, which are either of large size or small and numerous, may vary according to the shape of the plugs or masses of cells that accumulate in the connective-tissue framework or stroma—which are sometimes round or oval, long and narrow, or a combination of both—in different tumors. From these variations arise the acinous and tubular cancers of Billroth. Connective-tissue fibers infiltrated with round cells make up the stroma. Sometimes the amount of connective tissue is very small, there being often only a few fibers forming the trabeculæ which separate the alveoli, and then the plug-masses exist in greater numbers. Round cell infiltration is extensive in the periphery of the tumor.

The cut surface of the tumor shows the absence of a capsule or defined border, but a general infiltration into the tissues; it is fleshy and succulent, and of a grayish-white color, over which light striæ branch out. With the progress of the cancer the epithelial elements continue to multiply, and finally, after lymphatic, blood-vessel, and visceral involvement take place, large areas are changed to a soft cellular mass supported by only a delicate fibrous stroma. The tumor is richly supplied with blood-vessels, the growth is very rapid and it attains large dimensions in a short time. It is soft or elastic to the touch, of a rounded or hemispheric contour, and often softened and fluctuating spots are palpable. Suppuration in a malignant growth is very rare, but Bloodgood has observed abscess formation in two cases of medullary carcinoma. It is stated that the average duration of life is about a year, but this may be materially shortened and especially if the disease arises during pregnancy or lactation, when a few weeks may terminate existence.

(*b*) *Carcinoma Simplex.*—This variety occupies an intermediate rank between medullary and scirrhus carcinoma, from both a clinical and an histological standpoint. It constitutes an uncertain group of tumors in which the epithelial and connective tissue elements are about equally divided, and represents a percentage of from fifteen to eighteen (Finney).

(*c*) *Scirrhus Carcinoma* (*Hard Cancer*).—In this variety the connective tissue largely predominates over the other elements of parenchyma, and gives the characteristic hardness to the tumor. Here we find the carcinoma cells few in number and of small size,

and sometimes clustered together; the alveoli are generally spindle-shaped or ovoid, and are distributed about in an irregular manner. At an early stage of the growth the single layer of epithelial cells lining the small clusters of the acini assume abnormal proliferation; and these new or cancer cells crowd the acini and ducts producing the so-called epithelial nests. The basement membrane of the acini gives way under this pressure and the cells break through the walls of the glands, and, thus liberated, they infiltrate the surrounding stroma and lymph spaces. In the neighborhood of such acini numbers of alveoli are seen between the meshes of the connective tissue. The proliferation of connective tissue is pronounced, and much in excess of the epithelial cell growth, which last proliferates slowly, and even in a well-advanced growth the alveoli are often not entirely filled with cells. In the more typically arranged portions of the tumor is found a dense cicatricial-like tissue consisting of strands of connective-tissue fibers with sparsely scattered cells in slender and elongated bunches. This is the characteristic formation of the *atrophic or withering scirrhus*, the

Fig. 1128.—Unoperated Scirrhus Cancer of the Left Breast of Eighteen Years' Standing. (After Clopton; Mudd, Am. Practice of Surgery.)

highest type of scirrhus formation. In this type the progressive contraction of the newly formed tissue compresses the cells and arrests their growth, and prevents the blood-vessel formation. The squeezing or pressure causes the cells to be absorbed, or to degenerate and calcify. This cell degeneration proceeds at an equal rate with the growth of the neoplasm, the breast withering or shrinking, and thus leaves no palpable tumor.

In gross appearance a section of such a breast shows a central band or mass of white fibrous tissue, continuous with the retracted nipple above, containing remnants of ducts. Branching out from this mass into the remains of the gland and adipose tissue are a few bands of cicatricial tissue. A microscopic section presents the appearance of dense scar tissue, with scarcely any evidence of glandular structure; and the condition closely resembles the chronic atrophic mastitis of Billroth.

Scirrhus is the most frequent and least malignant of the glandular types of carcinoma on account of its few epithelial elements and its slow development; and the extreme type of the disease or atrophying scirrhus is still less malignant. It is variously estimated as occurring in the proportion of sixteen to fifty per cent.

These growths may occupy any portion of the breast or the nipple. There are no material facts as to the etiology of scirrhus, although it has been stated to be one of the types of malignant transition of chronic cystic mastitis, of benign growths, and of Paget's disease of the nipple.

Atrophic scirrhus is more often encountered in elderly women, sixty years or older, and those of feeble constitution and spare build. The course of this form does not differ from scirrhus in general; the increase is slow, often extending over years. In the late stages the skin adheres and ulcerates, the disease now seems arrested, and the ulcer contracts, becomes indolent, and assumes a deep red rose color. There is a scant discharge, little pain or other discomforts are experienced, and the general health remains undisturbed. These conditions may exist without change for years.

In early cases the complete operation should be practised. But, inasmuch as this variety of cancer is of slow growth and the average percentage of cures low, in certain advanced cases it may be the part of good judgment to postpone operation until the progress of the disease and the comfort of the patient actually require it. Occasionally in cases of atrophic scirrhus operation has been known to precipitate a rapidly fatal course.

Carcinoma in the *male* breast generally arises from the ducts of the gland and but seldom from the acini; and the embryonic or rudimentary condition of the gland in the male furnishes an easy explanation of this fact. All varieties of carcinoma have been observed, but the scirrhus form is by far the most frequent type in the male gland. In Warfield's group of twenty-six cases, eleven of them were scirrhus; and in 100 cases Williams found eighty-eight to be scirrhus, three encephaloid, six tubular, and three of the cutaneous squamous cell variety. It should be noted here that the male breast seems to be particularly prone to the squamous and melanotic types of cancer, which is probably due to the fact that the male mamma is generally more liable to cutaneous growths.

2. Adenocarcinoma (Malignant Adenoma).—The term adenocarcinoma is applied by Halsted to a group of cancerous tumors where there is an evident pedunculation or constriction at the base of the growth which gives it a prominence on the surface. It includes those types of cancer which manifest a disposition to produce glandular structures in the malignant tissue, the microscope showing large acini containing masses of epithelial cells surrounding a central cavity. Among these Halsted places villous cancer, and the duct cancer of English writers. Adenocarcinoma is rare (three to five per cent.) and only mildly malignant even when of exuberant growth with skin ulceration, to which condition it has a decided tendency. The malignancy seems to be still further reduced when the pedunculation is pronounced. Infection of the axillary lymph nodes is infrequent. Halsted obtained seventy-five per cent. of cures after operation in this variety. Furthermore, it has been frequently observed that with the progress of the growth there is a disposition for the adenomatous structure to disappear and give place to the common carcinomatous tissue. As to etiology, these adenomatous forms of cancer seem to have their origin in senile parenchymatous hypertrophy (chronic mastitis) or in the benign tumors, the cystic type especially, more often than any other form of malignant growth.

3. Colloid Carcinoma.—This form of carcinoma is extremely rare. It is estimated at from one-third to three per cent.; S. W. Gross gives it 1.34 per cent. of all breast tumors; and Warren has seen but three

specimens in a wide experience. The chief characteristic is the formation of colloid or mucin between the epithelial cells and the stroma. The alveoli are usually round and appear to be greatly distended with a gelatinous or colloid material, and the trabeculæ of the stroma are thin and translucent. The colloid is either transparent or homogeneous, or it may be striated, and is apparently developed at the expense of the cells of the alveoli—the intra-alveolar pressure thus producing degeneration of the contained epithelial cells. The process should be regarded rather as one of degeneration than a separate type. The malignancy is very mild.

Macroscopically the tissue is transparent and gelatinous, the surface of a section of the tumor being not inaptly likened to the interior of a grape or plum.

become involved in the carcinomatous process; and in no instance coming under his observation did carcinoma appear as a primary lesion, but always secondarily in the gland substance close to, but with a distinct bridge of apparently healthy tissue separating it from, the original skin affection. Thus the first conception of the pathology was that the primary skin affection represented the same precancerous state of the epidermis that is seen in the "paraffin" and the "chimney sweep" types of cancer, or similar to keratosis of old age, and which, at first localized on the nipple and areola, finally extended to the ducts and acini of the gland and progressed as a mild form of cancer. A more accurate definition by Cumston is, that it is a chronic pathological process of the skin of the areola and nipple associated with

Fig. 1129.—Paget's Disease of the Nipple. (After Fordyce; Mudd, Am. Practice of Surgery.)

4. Malignant Papillary Dermatitis (Paget's Disease of the Nipple).—This is a rare, chronic affection of the nipple and areola, eventuating in carcinoma of the mammary gland, and known by the name of its author, Sir James Paget, who first brought it to the notice of the profession in 1874.

The *pathology* of this disease has been one of the vexed questions in medicine, but now the majority of pathologists have about definitely assigned it to the ranks of the carcinomas. It was described by Paget as an eruption—a chronic eczema—beginning on the nipple and areola which continued to bear the characters of such even after the affected skin had

carcinoma in the breast gland. Jacobaeus asserts that the cancer may exist either as a superficial spongy mass in the retracted nipple, or it may arise within the gland, or again that both of these conditions may be present. In this connection the case reported by Kyrle is interesting: This was a married woman, thirty-nine years of age, affected with an adenocarcinoma of the breast, the nipple and areola of which presented a typical picture of Paget's disease. The disease had existed for a year and a half, and, in addition, there was a walnut-sized growth in the depths of the mammary gland. A careful microscopical study of the tumor and the diseased

areola indicated that the breast tumor was the primary condition, which had advanced in a retrograde direction through the nipple producing a secondary carcinomatous infection of that organ and the surrounding areola.

The disease is regarded by Ehrhardt, Karg, Matzenauer, and Benjamin, as a primary skin carcinoma. Thin states that it begins in the mouths of the lactiferous ducts as a slowly progressing carcinomatous process, which at an early stage causes irritation in the dermal tissues of the nipple and areola, and finally, the cancerous changes being long established in the ducts, extends backward into the mammary substance. Jacobaeus definitely decides from his investigations that Paget's disease is from the very outset a carcinoma arising from the glandular epithelium of the milk ducts. Both Schambacher and Ribbert hold to the same opinion, and assert that the morbid process must be accepted as a carcinoma arising within the nipple; and progressing *pari passu* with this infiltration are the inflammatory or eczematoid changes in the skin of the nipple and areola. Tschlenoff maintains that it represents an independent form of cancer of the skin, and that its pathological anatomy presents every appearance of cancer, the chief feature being found in the presence of Paget's cells which are not usual in other cutaneous diseases. These cells were formerly supposed to be psorospermia, but are now known to be peculiarly transformed epithelial cells. Thus it seems to be fairly well conceded that the so-called Paget's disease is not an eczema incidentally associated with carcinoma, but a degenerative process—a true carcinoma —from the beginning. It occurs in both men and women, and in addition, dermatological literature would indicate that the disease is not confined to the nipple and areola, but that a similar condition may exist in various portions of the body. After the breast, it appears that the male genital organs are next most susceptible, but it has been found on the vulva, umbilicus, perineo-anal and gluteal regions, the axilla, lips, and nose.

Paget, Porter, and more recently Thin, have studied the histological changes. The first stage appears as a keratosis of the superficial dermal layers, the epidermic cells together with the cells of the rête, more particularly those interposed between the papillæ, are largely increased in numbers. By this means the epidermis is thickened and elevated in crusts, and the interpapillary epithelium projects more deeply into the cutis vera. There is an increased vascularity of the affected area and the true skin is greatly infiltrated with small round cells. Early in the carcinomatous stage an epithelial growth is seen involving the corium and its glandular structures, the sebaceous and sudoriparous glands, and the ducts of the mamma. The ducts are crowded with pavement epithelium cells, and as these cells grow, the walls of the smaller ducts yield to the pressure and the growth goes on to invade the stroma of the gland. The growth preserves the type of epithelial or epidermoid carcinoma, and involvement of the lymph nodes occurs at a late period of the malady (Warren).

Symptoms.—The disease is found in both sexes; but it more often occurs in women beyond middle life, from forty to sixty years, after the lactation period, and is rarely found in those who have not lactated, or in young unmarried women. It is said to affect the right breast three times as often as it does the left breast. It is essentially chronic in its course, varying from two or three years to as long as ten or fifteen years. The patient commonly first experiences a smarting and itching in the nipple area, which is soon followed by an inflammatory or eczematoid condition, commencing on the nipple and spreading in a circle over the areola and adjacent skin. The axillary region becomes affected. The appearance is that of a raw surface, finely granular, and of an intensely red, florid hue, as if the entire thickness of the epidermal layer was removed, attended by a clear yellowish, viscid discharge. In other instances it is covered over by a yellowish crust, and in yet other cases islets of new epithelium are present. The indurated, parchment-like skin is a valuable diagnostic symptom; the nipple retracts at an early stage; the axillary region becomes involved; the general health remains unaffected. The skin condition may continue for years, ordinarily two or three years, before involvement of the gland is recognized; although, as Jacobaeus has shown, the microscope will disclose the existence of cancer long before a tumor becomes palpable.

Treatment.—The treatment should be instituted early and should consist in total removal of the breast as soon as the diagnosis is made. When distinct involvement of the gland exists, the radical operation for carcinoma of the breast should be performed, including removal of the pectoral muscles and dissection of the axillary space.

5. Cancer Cysts.—There is occasionally mentioned in the extensive literature of mammary carcinoma a peculiar cystic formation which has been described as cancer cysts. These cysts are not only the rarest but the most malignant of all forms of breast cancer. They ordinarily occur before the age of forty years, and like simple or involution cysts of the breast they are of rapid development and may be located in any segment of the gland. But, on the other hand, they are unlike them in being single, in having somewhat thicker walls, in their continued rapid growth, and in that they always contain blood, which latter is a symptom of much importance. Moreover, they exhibit an intimate relationship with lactation and mastitis, as shown by Halsted and Bloodgood to exist in the cases occurring at the Johns Hopkins Hospital, thereby again differing from both the simple cysts and the cysts associated with papillomatous ingrowths.

Prompt and complete removal of the breast, muscles, and axillary glands is the necessary surgical procedure.

Cancer of the Axillary Border.—Warren describes a form of cancer under this title, which starts as a lenticular nodule in the cutaneous fold outlining the anterior margin of the axilla. It appears at first as an infiltration of the true skin about the size of a silver quarter of a dollar, having a depressed center and well-defined rim or border, eventually affecting the mammary gland, and then involving the axillary glands. Warren had seen three cases at the date of his writing. Death from metastases occurred in one case, and the other two were living and well three years after operation.

Multiple Carcinomas of the Breast.—Multiple primary cancers of the breast are rare. The occurrence of carcinoma in both mammary glands at the same time has been estimated at from three-fourth s of one per cent. to five per cent., and is oftener met with than the simultaneous appearance of several separate cancerous points or foci in the same breast. Under these circumstances it seems reasonable to conclude that such deposits generally arise from malignant degeneration of benign conditions already existent in the breast, as in, especially, senile parenchymatous hypertrophy (chronic cystic mastitis), or in benign growths. LeDentu and Morestin report an interesting case of the former condition undergoing multiple carcinomatous transformation. The occurrence of cancer in one mamma with the existence of benign or carcinomatous growths in the companion gland are more frequent, as Coley has shown. The appearance of primary mammary cancer simultaneously with primary carcinoma elsewhere in the organism, more particularly in the ovary or the uterus, must be regarded as rare. The instances of this last

condition are rather more suggestive of possible confusion with metastasis from these localities to the breast.

Secondary Carcinoma.—Secondary carcinoma of the mammary gland is but seldom met with. When such occurs, it arises either from extension by continuity of tissue from primary disease in adjacent structures, or by transference from another locality more or less distant. Metastasis from other organs is very rare, and the most frequent source is from carcinoma in the other breast.

Symptoms and Course of Mammary Carcinoma.—In order to obtain a just estimate of the clinical course of carcinoma of the breast it is necessary to separate the disease into the two accepted clinical classes, that is, the acute and the chronic forms.

Acute carcinoma mammæ (aigu du sein, Charbonnier) was first described by Volkmann in 1875 under the title of *mastitis carcinosa*, and since then various authors have written on the subject and reported cases under the several designations of acute cancer, acute brawny cancer, inflamed cancer, and cancer mastitoides. Roger Williams also graphically pictures the affection, and in the past few years Rodman, Schumann, Gibbons, Nassau, W. J. Taylor, and others, have reported cases.

The disease must be considered as very rare, although less so than was formerly believed, and closely resembles acute mastitis. It represents a virulent or *foudroyant* type of carcinoma of the breast, producing intense irritation of the tissues accompanied by a rapid infiltration of round cells and inflammatory symptoms. Both the scirrhus and medullary types have been observed. The invasion is sudden and the progress is extremely rapid, with all the symptoms of acute inflammation. There may exist in the beginning a small nodule or indurated mass, but ordinarily it commences as an acute inflammatory and diffuse process, without any definite palpable tumor, and the entire gland is enlarged, firm, and painful. Sometimes there may be a feeling of fluctuation. The subcutaneous veins are enlarged and the skin is edematous, brawny, reddened, and adherent, presenting a striking resemblance to acute mastitis, and for which it has been mistaken. The infiltrated and brawny skin may early show small abscesses and necrotic areas, and the inflammatory process may extend to the surrounding integument of the thorax; but a general breaking down of the whole breast has not been observed. A condition of "orange skin" or "pig skin" has been noted; and the nipple is usually, but not always, retracted. There may be both local and general elevation of temperature. The disease rapidly advances, involvement of the axillary and supraclavicular glands and general metastasis or carcinomatosis occurs at an early stage, the toxemia is profound, and death results sometimes in a few weeks but seldom later than a twelve month. It is commonly associated with pregnancy and lactation, and, in consequence, is encountered in young women and before late middle life, that is, during the period of the physiological activity of the gland.

A section of the tumor shows a rather firm and fibrous tissue, of a dark red or purplish color, and sometimes with both small abscesses and hemorrhagic areas scattered over the surface. There may be also necrotic spots, and in some places the abscesses may be of rather large size. The skin shows edema and induration which may extend some distance beyond the limits of the breast.

The only diagnostic difficulty is in confusing the disease with acute suppurative mastitis, from which the differentiation is by no means easy. In fact the distinction may not be made until after operation or a section of the growth is submitted to the microscope. However, any supposed case of mastitis that does not yield to treatment within a comparatively few days or in which abscess is not promptly determined, especially if occurring during pregnancy, should be viewed with suspicion. In acute cancer it is probable that the temperature is not so high as in suppurative mastitis, and, again, in acute cancer the inflammatory process is probably more diffuse, the skin is more extensively implicated, more brawny and generally adherent to underlying tissues. Early implication of the lymph nodes may be present in both affections.

The course is progressively downward and uniformly fatal, and unless the diagnosis is quickly made, treatment is without avail. Therefore, early diagnosis and prompt radical removal of the breast, muscles, and infected axillary and supraclavicular glands offers the only hope in these cases.

The onset of the chronic form of carcinoma is ordinarily slow and unnoticed. The growth may remain unrecognized for months and its discovery be a matter of mere accident. The discomfort produced by pressure of the clothing or some slight traumatism may first lead to its notice, or, less frequently, the individual may experience pain, either sharp and cutting or dull in character, which attracts attention to the breast and the presence of the tumor. A small nodule or mass of extreme hardness, ill-defined in outline, and movable with the gland is now disclosed on palpation, and which is practically without pain, insensitive, and evincing but little tendency to enlarge. The health of the patient is also unimpaired at this stage. This seemingly quiescent condition may undergo scarcely appreciable change for a period of weeks or even months. The rapidity of growth, however, is influenced by the character of the cellular elements and the degree of malignancy of the growth. After an indefinite time the tumor indicates activity, and progressive increase in size now becomes quite apparent. The pregnant state, lactation, or injury may greatly accelerate the rapidity of its growth and general progress. The effect of the stimulus of pregnancy upon mammary cancer is well understood, and under such influence it has been known to assume a virulent or fulminant type of malignancy with a violently rapid course. Cheesman has recently related two cases exemplifying this condition in a most typical manner.

The course of the disease varies. The patient may succumb in the brief period of a few months after its discovery, or may continue in a fair state of health for a number of years. It is of comparatively rapid growth in young subjects, but in those of advanced years it grows slowly and lymphatic involvement may be deferred for years. The atrophic form of scirrhus has been known to exist as long as ten, fifteen, and twenty-four years, and the affected individual may finally die from some other malady. The length of life in non-operated cases was given by Cooper at from two and one-half to four years; and according to Gross the average duration of life is 28.06 months; and other writers give it from ten to twelve months. Probably the last represent the most accurate figures, but, as already shown, these are susceptible of marked variations.

Carcinoma is of much slower growth in the male than in the female. The average duration from the time when first noted until coming under the observation of the surgeon is stated by Williams as 29.5 months, and by Finsterer as eighteen to twenty-five months. But it may run an exceedingly rapid and virulent course as demonstrated by Moore's case of only two weeks' duration, the case of Finsterer of two months, and that of Speese of three months.

As the disease progresses the integument over the mass becomes slightly depressed or pitted at multiple points, the so-called "orange skin" (peau d'orange) or "pig skin," which is caused by the implication of the ligaments of Cooper in the morbid process. These fibrous bands or processes afford support to the gland structure together with lymphatic radicles, and when

they become infiltrated with cancer cells and thereby destroyed, the resulting cicatricial tissue contracts and depresses the skin in the fashion described. This dimpling is the first step toward cutaneous infiltration, softening, and ulceration, and which, if surgery does not intervene, occurs at one time or another in the history of the tumor. Adhesions of the tumor to the skin, muscles, and thoracic wall, as shown by its fixed condition, indicate invasion of these structures, and are stated by Rosenstern to

Fig. 1130.—Retraction of the Nipple with Marked "Peau d'Orange," in a Case of Carcinoma of the Breast. (Mr. Sampson Handley in a System of Surgery, edited by Choyce and Beattie.)

occur in eighty-four per cent. of the cases. The ulceration may be superficial, but it is usually deep and crateriform, with irregular and indurated edges, necrotic granulations covering the base, and the exudation of a watery blood-tinged and foul-smelling discharge. Pain may be either insignificant or intense, and repeated hemorrhages may occur from the ulcer surface.

It has been shown that ulceration occurs in the male mamma in about thirty per cent. of the cases.

Retraction of the nipple follows when the neoplasm is situated in the retro-areolar space or in the near neighborhood of the nipple, and has been estimated to take place in about twenty per cent. of the cases. Nipple retraction is more frequent in the male breast, in which it is said to occur in fully one-third of the cases.

Lymphatic involvement may be early or it may be late. The glandular group ordinarily first invaded is that situated just beneath the axillary edge of the pectoralis major muscle, the infection then passing on to the deeper nodes of the axilla. Often these glands are bound together and can be felt as conglomerate masses, and when single they are usually longer and more distinct than where simple inflammation causes the hypertrophy.

When the lymph nodes surrounding the large vessels are extensively infected pressure interferes with the venous blood return, and swelling of the arm and hand, often to an extreme degree, is the consequence. Infection of the supraclavicular glands is a much later manifestation; and extension to the bronchial glands takes place about the second year. Axillary involvement is stated by Finney to occur in eighty-four per cent., and was demonstrated in from ten to thirteen months, and the supraclavicular nodes in ten per cent. at from eighteen to twenty-one months after the discovery of the tumor, and eight months after the axillary infection. In the male breast axillary glandular involvement is stated to be present in from sixty to seventy per cent. of the cases.

As has been already mentioned carcinoma shows a positive predilection for the upper hemisphere of the gland and the upper and outer quadrant in particular, and which applies equally to both the female and the male breast. Therefore the route of infection more commonly leads in the direction of the axilla. But when the primary lesion is located in the inner hemisphere of the gland the extension is toward the sternum; nodules form at the sternal border and these communicate with the mediastinal glands and finally the infection may spread to the pleural surface of the intercostal region.

In certain extremely malignant forms of breast cancer a retrograde lymphatic dissemination in the skin and tissues of the chest takes place, to which Velpeau applied the name of *carcinoma en cuirasse*, and which, fortunately, is now rarely seen. The cutaneous metastasis is often very extensive, the infiltration involving the larger portion of the chest surface. The integument becomes hard, wooden-like, and nodular, forming adhesions with the deeper tissues of the thorax, and encasing the chest like a cuirass. This causes great distress to the sufferer, and may so impede respiration as to produce death from suffocation.

Cancer deposits through the superficial lymphatics may be still more widely disseminated, as seen in the form known as "lenticular cancer," where the skin of the chest, abdomen, and back is covered with

Fig. 1131.—Cancer en Cuirasse, Including Both Breasts. (From the collection of Dr. Franz Torek, Mudd, Am. Practice of Surgery.)

numerous nodules varying in size from a lentil seed to a hazel nut or larger.

Charcot has described a most painful morbid state due to metastatic deposits in the spine, producing pressure on the cord and spinal nerves, which he calls "paraplegia dolorosa." William Osler has also made a valuable contribution to this subject. Appreciating that secondary transference of cancer cells may occur at an early age of mammary carcinoma, Osler urges a careful examination of the breasts for unrecognized

growths in all obscure spinal, visceral, and bone lesions.

Internal matastasis may occur when the breast tumor is quite small and apparently unimportant, but usually it is a later manifestation and takes place at about the expiration of two years. From twenty-three to thirty-eight months has been mentioned as the usual limitation. The liver and pulmonary area are the most frequent seats of secondary deposits, and then follow the stomach, the companion mamma, the spine, the sternum, the long bones (femur and humerus), the cranium, and the central nervous system, as respectively mentioned.

Secondary internal deposits occur in about the same order in the male. In a collection of eighty-eight cases, Williams noted bone metastasis in five of them, embracing the clavicles, tibiæ, vertebræ, and skull.

A condition of cancerous cachexia or toxemia often exists, and is caused by the absorption of the poisonous products formed by tissue destruction during the course of the disease. This more often accompanies advanced cases with metastasis, but may be encountered while the tumor is seemingly localized. The anemia may be intense and is associated with emaciation.

Diagnosis.—In advanced cases with well-defined symptoms the nature of the disease is unmistakable, but in the early stages, when a decision for or against malignancy is of the utmost importance, the diagnosis may be beset by great difficulties and not infrequently is a matter of impossibility. In many instances the previous history sheds little or no light on the subject, and generally the existence of a small indurated area or growth is the one material fact in the case. Here every possible phase of the case must be considered, and a careful physical search made of both breasts, the axillæ, and the cervical regions. The breast, nipple, and areola should be closely inspected, comparing them with the sound side, inspecting the breast in different positions as may be required, and the slightest variance from a normal appearance duly noted. The contour, mobility, consistency of the gland substance, and the sensitiveness to pressure, need to be attentively observed. The existence of adhesions, superficial and deep, is sometimes disclosed by gently dragging the breast in different directions, and also by drawing the skin away from the gland, or lifting up the breast from the chest wall by grasping it at the circumference. Standing behind the sitting patient and with the pendant breasts resting in the palms of the hands, the weight and size of the two organs can be estimated and compared. In the same position the entire breast is palpated by the fingers and the open palm. If a distinctly palpable growth be present, the outline and shape, whether firm and hard or fluctuant, whether movable within the mammary tissues or only to be moved with the gland, are important facts to be learned for the correct differentiation of the case.

When the disease is somewhat further advanced the classical symptoms are present, namely, a tumor in the upper hemisphere, and oftener in the outer quadrant, which is fixed to a greater or lesser extent, retracted nipple and multiple skin dimplings, glandular enlargement, varying degrees of pain but more frequently of a lacinating type, and in the later stages metastases and cancerous anemia. Enlargement of the lymph nodes is not pathognomonic of cancer, for they may accompany benign growths and inflammatory conditions, and besides the glands may be infected with carcinoma and yet not palpably enlarged, or even may not be felt. Nipple retraction is an early symptom only when the growth is situated near the nipple, and if it occupies the peripheral areas of the breast retraction of the nipple is either absent or of late appearance. It should be borne in mind, however, that the position of the nipple may be changed by injury or ulceration, and also in certain inflammatory lesions of the breast. Of much more positive diagnostic value are the punctate depressions of the skin, which are readily demonstrated by drawing the breast to one side and thus putting the tissues between the breast and the skin on the stretch. This symptom is one upon which Halsted places great reliance.

When a positive diagnosis cannot be determined, direct examination of the tumor should be made through an exploratory incision, and the radical operation immediately proceeded with if it prove to be malignant.

Hemolytic reaction in the early differentiation of cancer is a diagnostic measure that seems to promise definite aid in these cases. The researches of Kellnig, Rosenbaum, and the later work by Crile, on the destructive effect upon the red blood cells taken from a healthy individual by the blood serum from cancer cases, is so important that the method should not be neglected in clearing up the nature of obscure breast tumors.

Prognosis and Mortality.—The prognosis of mammary cancer is influenced by many conditions. The cases not operated on, although having but a brief span of life allotted to them, naturally differ in the time of the fatal day—varying from a few months to two decades or more, with an average of about two and a half years. The cases subjected to the knife, notwithstanding the radical methods employed, cannot be considered as altogether exempt from local recurrence. The three year safety limit of Volkmann is no longer tenable, for even the lapse of five, ten, twenty, or more years after operation has been followed by local reappearance and a cancer death. The assertion that a patient is cured signifies that the cancer element has been wholly eradicated from the system, and in the present status of the cancer question this is a matter of serious doubt.

The prognosis largely depends upon the pathological type or degree of malignancy of the tumor. Thus, as would be expected, medullary carcinoma gives the worst average results and is the most rapidly fatal form, although this differs from the experience in at least one clinic (Johns Hopkins Hospital). Next in the order of malignancy are scirrhus carcinoma (35.5 per cent. of cures), malignant papillary dermatitis, adenocarcinoma (75 per cent. of cures), and colloid cancer, the two last mentioned being generally recognized as the less malignant of the carcinomas. It has also been shown that age markedly affects the malignancy of mammay carcinoma, it having been observed that the older the individual at the time of the appearance of the neoplasm the less virulent was its course. Again, it is claimed that there is a greater tendency to recurrence in stout and obese women than in those who are thin and of slender build.

The shorter the duration of the disease, that is, the earlier operative intervention is resorted to, the greater is the prospect of permanent relief. This fact has been demonstrated in a positive manner by Warren, who showed that of those cases operated on before adhesions occurred seventeen per cent. were cured, but after adhesions had formed the recoveries fell to five per cent. It is well said, that incomplete operations in recent cases yield better results than complete operations in late cases. Where the tumor is adherent to the thoracic wall, and in those cases where extensive cutaneous lymphatic dissemination exists the prognosis is invariably bad.

Implication of the axillary and other lymphatic glands decidedly affects the prognosis. In the cases where the axilla was not infected Warren estimates his cures at sixty-four per cent.; and Bloodgood states that in Halsted's clinic only seven per cent. of the patients who had infected cervical nodes were apparently in good health at the expiration of three years.

The length of life in cancer of the breast has been materially increased with the developments of

modern surgery and the more radical technique in the operations devised for its removal; and the outlook is steadily becoming more hopeful. The immediate operative mortality has been greatly reduced. In Billroth's early cases the fatality following amputation of the breast for cancer was twenty-three per cent., whereas today it has fallen to between one and two per cent., and in the hands of many individual operators it stands at nil.

In those cases where the disease returns in less than three years the average length of life has been increased by ten or twelve months over non-operated cases, that is to say, they live on an average from two and one-half years to three and one-half years; and the general average of life after operation has been stated to be from fourteen months to twenty-five months. Even with the three-year limit after operation as a standard, Cheyne gives fifty-seven per cent. of cures; and the general average, in the hands of competent surgeons, is placed at forty per cent. But, on the other hand, Barker has shown that of those persons who were seemingly well three years after operation thirty per cent. succumbed to cancer; and Smith found the percentage of cures to be forty-three per cent. with the three-year limit, but only seventeen per cent. of these remained well after this period. Halsted gives forty-one per cent. apparent cures and fifty-two per cent. local cures under the same limitations. Finsterer in an analysis of 606 cases of mammary carcinoma from Hochenegg's clinic, states that the permanent cures had risen from 12.5 per cent. before 1903 to 24.64 per cent. in 1907. This increase was ascribed to the more extensive surgical procedures, especially in the removal of wide areas of skin and the clearing out of the supraclavicular fossa. He refers to cures in some cases where the cervical glands were already infected. Quite recently Lewis S. Pilcher has reported twenty-six cases of patients, operated upon by himself, who have remained free from recurrence since operation to the time of writing (1912) or as long as they lived, during periods of five to twenty-five years. Several of these patients had infected cervical glands.

Local recurrences vary with the completeness of the operation, which is practically equivalent to the extensiveness of the tissues removed. In the older operations the local recurrences were estimated at eighty-five per cent. In those cases where the modern operation was performed but did not include excision of the muscles, local recurrence is stated to be between forty-five and fifty-five per cent.; whereas with the more radical or complete operation, local return of the disease is given as six to nineteen per cent.

As a fact of peculiar interest, and in contradiction of the opinion that no positive benefit is possible without extensive procedures, it should be noted that Sir H. C. Cameron mentions two patients who survived for twenty-two and thirty-three years respectively after a simple amputation of the breast, without any interference with the axilla. Not a few similar cases have been reported.

Recurrence *in loco* may take place any time after operation, but it is more frequent within the first six months (forty to sixty per cent. and fully fifty per cent. of these in the first three months), after which period the rate rapidly and steadily declines, and regional recurrences are comparatively rare after the expiration of one year. The statement is made that two per cent. of local recurrences take place after three years, but this is considered a very low estimate.

Metastases are said to take place in seventeen per cent. of all cases and to occur early and without local reappearance in fully one-third of these.

The prognosis after multiple operations, although much less favorable than after the primary operation, should not be regarded as entirely hopeless; and the second or third operation may be undertaken with the possible expectation of securing temporary benefit at least. This statement applies particularly to those cases in which there is a long interim between the recurrences. Walbarst mentions a case where recurrence took place nine months after the first operation and again twenty-two years after the second operation. In a case reported by Hutchinson four operations were performed, which included removal of the second mamma, and twelve years later there was no evidence of reappearance. Frank W. Murray refers to the case of a woman under his observation who was well twenty-two years and six months after the first operation and thirteen years after the last operation, three operations being performed. Johnson reports a patient who was well twenty-six years after operation and then had recurrence; and W. S. Schley mentions a case operated on for recurrence thirteen years after the primary operation. L. S. Pilcher has recently published cases of recovery after secondary operations for recurrences, including several interesting ones of bilateral removal of the breast, the second breast becoming affected as a late recurrence.

Operation employed as a palliative measure in apparently hopeless cases is occasionally attended by surprising and gratifying results, and in some instances has been followed by years of health. In thirteen cases of this character Warren operated by the radical method with the result that one lived eight years, three lived three years, and one survived one year.

The late recurrences, several years after operation, which are observed with a fair degree of frequency in the female breast, are unusual in the male. In the greater number of male cases recurrence takes place at a much earlier date—only a few men have been reported as living and well from four to eight years after operation. Manger's statistics of male cases show that a fatal result took place in seventy per cent. of the cases from general recurrence or metastasis, and that local return occurred in nineteen of seventy-two cases within periods ranging from a few months to five years. Finsterer succeeded in finding only six reported cases where it could be definitely asserted that recurrence had not taken place, and of these, two were living after eleven and twenty-one years respectively; Blodgett's patient lived five years; and the patient of Speese was alive three years after operation.

It is interesting to mention that Bryant and Nunn report a case in which spontaneous disappearance of individual cancerous nodules took place, which had recurred in the cicatrix following operation.

Treatment of Mammary Carcinoma.—The ideal treatment of cancer of the breast would be its prevention, and while such an achievement is but a dream of what the future may bring forth, still much can be done toward lessening the frequency of its occurrence and limiting its progress. To this end the timely removal or correction of those affections of the organ which are known to hold an etiological relationship to the disease should be attempted. This in turn requires the cooperation of the general practitioner, who should request surgical counsel at the earliest moment in all breast tumors coming under his notice; and what is equal if not paramount in importance to every other effort, the instruction of the public as to the probable danger attached to so-called "lumps" in the breast, and the necessity for promptly seeking medical advice for their treatment.

The involution changes of the senile breast, occurring as they do at the time of life when cancer most often begins, should always be regarded as a menacing condition and viewed with suspicion. It would be a definite step in advance if the breasts of every woman who has reached the climacteric stage of life could be subjected to careful examination at stated intervals. Advantage could be then taken of the first indication of pathological change, and the entire breast or the morbid formation, as the case might be removed without delay.

Inflammatory lesions of the breast, that is the several forms of mastitis, have been sufficiently often followed by cancerous transformation to demand close watching as to their course and chronicity. Prompt excision of any indurated mass that has resisted the usual therapeutic methods and does not undergo resolution within a reasonable period should be the rule. It has been clearly demonstrated that cleanliness and proper attention to the breasts during pregnancy and after parturition will in a large measure prevent nipple infection and lactation mastitis, and such attention should always be the solicitous care of the obstetrician.

It has been shown that a large percentage of benign mammary tumors manifest, according to their cellular composition, a tendency to assume malignant degeneration; and, consequently, every neoplasm of the breast should be looked upon as suspicious, and kept under intelligent observation ready for prompt surgical intervention upon the slightest evidence of active change. In other words, as Finney has aptly expressed it, "No tumor can be adjudged so benign that it will never become malignant, and no tumor will ever be more benign than when first recognized. There is only one sure cure for any benign tumor, solid or cystic, and that is complete removal."

Unnecessary removal of the mamma is to be condemned, and, therefore, when an obscure growth is discovered in the breast every legitimate method should be employed for its elucidation. Direct exploration through an incision made down upon the mass will often reveal its true nature; or, if necessary, a section of the growth can be excised for immediate histological examination, and then the operation completed in the manner made necessary by the microscopic findings. Often quite a small incision will suffice for this information. These measures naturally are only available in a hospital with modern laboratory equipment. The removal of suspected tissue by the harpoon or punch for examination, and the practice of excising a specimen of the tumor and then closing the incision pending the microscopic study and a later secondary complete operation, are only mentioned to be discountenanced. The first is risky and does not afford the requisite information, and the second, in the presence of malignant disease, becomes a real danger by causing cancer autoimplantation and dissemination in the susceptible surrounding tissue.

Excision of the entire breast and its immediate microscopic examination is often a reliable method of diagnosis, and the operation can then be finished according to the disclosures thus revealed to the eye. This procedure can be adopted with satisfaction in many cases, its principal drawback being the possibility of needlessly removing an organ the seat of an innocent growth.

Operative Treatment; Curative.—Complete removal of the breast with all carcinomatous tissue, including the areas of possible infection, is the only treatment that offers the smallest prospect of a lasting cure. The paths along which infection travels from the original breast focus to the adjacent tissues together with those structures in which recurrence shows the greatest tendency to take place should be kept in mind, and the incision and other steps of the operation so planned as to embrace these structures—to pass well beyond the infected zone and only through healthy tissues. The skin of the breast, the adjacent muscles and fasciæ, and the axillary lymph glands are the structures in which the disease most commonly returns. The modern operation, therefore, has for its purpose not only the excision of the mammary gland but a wide dissection of all of these tissues. Halsted was one of the principal pioneer workers in this field, and to his painstaking investigations and surgical skill we are largely indebted for the radical operation for mammary cancer as now practised; but it should not be forgotten that Moore advised the routine removal of the entire breast for carcinoma as early as 1867.

Whatever incision is adopted it should be so planned as to widely circumscribe the skin over the growth, but, at the same time with ample provision for covering in the axilla, and to avoid restricting the functions of the arm as much as is consistent with the efficiency of the operative procedure. It is well established that local recurrences more frequently appear in the cicatrix or in the integument over the chest, and unless a wide sacrifice of skin is made reappearance of the disease is to be anticipated. S. W. Gross fully realized this danger and employed a broad circular incision, leaving the wound to heal by granulations. Rotter advised that the excision of skin cover the distance of three fingers breadth beyond the limit of the breast in the neighborhood of the growth. But the surgeon must be governed in this matter by the individual case and the extent of integument involved. Where adhesions to the tumor exist, or when the growth is peripherally located, the removal of a broader surface of the skin will be indicated. Lenticular skin metastases may preclude the possibility of removing all the infected skin, and the ultimate result in such cases is inevitably fatal.

The dissection should also include extensive removal of the fat surrounding the gland and extending up into the axilla. This is equally important, if not more so, than the skin ablation, and the fat should be thoroughly dissected away.

The investigations of Mr. Handley have shown that extension or permeation of cancer takes place more rapidly and directly along the fascial planes, and in confirmation of this we find that the pectoral fascia is invaded at an early date, before cutaneous involvement and even before there is evidence of adhesions with the growth. Its complete and wide extirpation, therefore, is one of the chief features of the modern operation. Volkmann first began to excise the pectoral fascia as a regular method in 1882, and Rotter recommended extending the practice to the fascia of the serratus magnus muscle and the upper portion of the external abdominal oblique and rectus muscles. In 1905 Mr. Handley advised that the usual incision be prolonged downward over the linea alba, the flaps undermined and the abdominal fascia excised as far down as a line running horizontally two inches below the ensiform cartilage, or lower if the growth occupied the inferior hemisphere of the breast. He states that while modern statistics indicate a decided diminution in the general recurrences, abdominal metastases seem to be increasing in proportion to the lessened thoracic recurrences, and refers to a series of 100 cases reported by Watson Cheyne in which there were fifteen visceral metastases. He further states that transepigastric abdominal infection often precedes invasion of the chest, and that in twelve per cent. it occurs alone without thoracic implication. In explanation of this he shows that the inner edge of the gland is only about one inch from the angle between the ensiform cartilage and the seventh costal cartilage, in which space and around the top of the ensiform cartilage the cancer-laden lymphatics of the deep fascia are separated from the subperitoneal fat by a single layer of fibrous tissue and may thus find ready communication with the peritoneum and its visceral contents.

It is probable that excision of the fascia without removal of the muscle or a part of the muscle is often a questionable procedure.

Removal of the pectoralis muscle was first performed and adopted as a regular part of the operation by Halsted in 1888, although in 1867 Banks had advised the practice in those instances where the muscle was already involved. The method gained universal acceptance after the publication of the observations of Heidenhain in 1889 together with the report of Halsted's series of cases in 1894. Heidenhain clearly

demonstrated the early presence of cancer cells in the pectoral fascia and muscle, and hence advised that the fascia with a layer of muscle be excised in every case, and when adhesions with the growth had taken place that the entire muscle be removed. The wisdom of this practice was later shown by a number of investigators who found solitary cancer deposits in the muscle even in early cases and before adhesions had formed. Excision of the major pectoral muscle admits of removal of the retropectoral glands and the fat in which they lie, which is important since they become infected at an early period. The same reasons apply to the excision of the pectoralis minor muscle. In opposition to this routine practice, J. B. Murphy declares that it is seldom necessary to sacrifice the pectoral muscle, and maintains that when the disease is seen at an early stage it has not passed beyond the fascial limits. However, the office of the lost pectoral muscles is soon largely supplemented by other muscles, and the natural movements of the arm are not greatly restricted. If the muscular sheath is stripped off without removing the muscles, the resulting inflammatory exudation may leave a stiffened condition which may be persistent and thereby materially interfere with the arm function.

The dissections of the muscles can be commenced either from below upward and continued out to the axilla, or by first dividing their tendinous insertions to the humerus and coracoid process and working downward and inward. Preference should be given to the latter method because it possesses the several advantages of cutting the blood-vessels and principal lymphatic channels during the very first steps of the operation, and thus lessening both the hemorrhage and the danger of forcing cancer elements further on into the lymph stream through manipulations of the tumor, and also on account of the greater facility it affords for the dissection of the axilla.

Clearing out the axillary pit of the glandular and fatty contents is another important step in the operation. It has been proven that the axillary glands are infected, in the large majority of the cases (eighty to ninety per cent.), even at a very early stage and before they are palpable, and they should be thoroughly removed at each operation. The higher up in the axilla the nodes are implicated the less hopeful is the ultimate result, and when the vein is encased in a mass of carcinomatous glands a cure cannot be expected. The axillary dissection should be carried out with care and thoroughness, and this is greatly facilitated by the exposure of the vessels as a primary step in the operation. Volkmann was the first to suggest removing the palpable axillary glands; but Küster was the first (in 1883) to advocate the routine evacuation of the axilla.

The lymph nodes just outside of the axilla, placed between the two pectoral muscles at the sternal edge, were found diseased eleven times in a series of thirty-three cases (Rotter), and may be infected at an early date. But authorities do not speak of them as of special importance.

The evacuation of the supraclavicular triangle and removal of the cervical nodes, either with or without division of the clavicle, in the early days of the operation was urged as a regular procedure by a number of surgeons. But at the present time it is employed only when these glands are distinctly diseased, although it has been stated that one-half of the palpable glands (ten per cent.) in this region are carcinomatous.

Drainage is generally advisable for the first forty-eight hours, to provide for the escape of the free wound secretions from the large raw surface. This is best effected by tubular drain and gauze wick through a stab wound in the dependent margin of the axilla, which admits of the suturing of the incision throughout.

The final step in the operation is the closure of the wound, but this is usually so extensive that the edges cannot be approximated in the regular way. In the early days this was left to heal by granulation, but now the majority of surgeons prefer to close it by some immediate method in order to secure the always desired primary union. This can be obtained by covering in the wound either by flaps designed as a part of the primary incision; by sliding skin flaps fashioned as a last step, after the breast is removed; or by skin grafting—immediate or secondary—after the method of Thiersch. The first of these procedures is the preferable, and can be ordinarily accomplished in a satisfactory manner by one or another of the several ingenious incisions suggested by different operators.

The treatment in the male differs in no respect from that in the female. Wagstaffe reports the removal of both breasts in a man for scirrhus.

Other Methods of Treatment: Palliative Measures.—The specific drug treatment of carcinoma of the breast is entirely obsolete. The many and much vaunted cancer remedies have proven not only useless but injurious, and the only justifiable medication is that which embraces tonic and supportive measures. Arsenic still retains the confidence of some members of the profession, but its remedial virtues reside probably in its tonic effects.

The injections of trypsin advocated by Beard have not confirmed the claims that were made for it. More recently the thymus gland treatment has been suggested, and favorable results from its administration have appeared from several sources. Gwyer believes that the chief beneficial effects are to be derived in those cases where an incomplete operation has been performed, and he states that in advanced and inoperable cases life may be prolonged and made endurable, and in still others the general and local conditions so much improved as to admit of operative intervention which otherwise was not feasible.

Fig. 1132.—Warren's Incision in Removal of the Breast for Cancer.

The Roentgen rays are practically without value in mammary carcinoma, although they are credited with possessing healing qualities in a limited number of early recurrences. It has also been claimed that this form of ray-energy was efficacious as a supplemental measure after operation in preventing recurrences, but the general results have been far from encouraging. Radium and the violet rays have likewise been tried and found wanting. All of these agents, however, may be employed for the relief of pain in advanced and inoperable cases, under which circumstances they have been used with marked and gratifying effects.

The fact that double oophorectomy results in bring-

ing about the menopause and associated involution of the mammary gland, long ago suggested this operation in cases of inoperable cancer of the breast, but the subject was first prominently presented to the profession by Beatson of Glasgow in 1896. Beatson recommended the operation on the ground that the ovaries were the organs responsible for the proliferation of epithelial cells in carcinoma mammæ, and the operation sprang into popularity and was widely practised. The early results seemed to be promising, many cases were reported as benefited, and even cures were claimed in not a few instances. Fifty-one cases were recorded by Roubaud with improvement in twenty-three, but in only three of these was it permanent, and it was without effect in the remaining twenty-eight cases. Lett's collection of ninety-nine cases gave material improvement in thirty-six per cent., and very decided benefit in twenty-three per cent., as indicated by relief from pain, diminution and even disappearance of the tumor, healing of existing ulcerations, betterment in general health, and prolongation of life. By excluding those patients past fifty years of age the improved cases rose to forty-one per cent. He claims that the most favorable age is between forty-five and fifty years, but that after fifty years the procedure is rarely beneficial. Stanley Boyd collected forty cases showing comparative success in thirty-five per cent.; and Abbe operated on seven cases with two encouraging results. At the French Congress in 1907 (Paris) Reynes of Marseilles reported several failures, all the patients subsequently dying from malignant cachexia; and at the same meeting M. Psaltoff of Smyrna related the history of two panhysterectomies which he had performed for the malady, both succumbing to extension of the disease. With this evidence it is clear that the results are not uniform, that it is justified in only certain cases and in individuals under fifty years of age, and that the operation cannot be classed as an established procedure.

In those instances where the cancerous infiltration is so extensive that it is impossible to eradicate all the diseased tissue by operation, and yet where this is the only available palliative treatment in the case, there should be no hesitancy in resorting to a radical operation for mental as well as physical alleviation. Such patients are always placed in a happier mental state; and occasionally the physical results are surprising, as exemplified by the cases of Warren already mentioned.

There are other more advanced cases with fetid ulcerations, agonizing pain, arm edema, and the patient demanding relief at any cost, where a radical operation is justifiable even though the benefits are small and of very brief duration; and in such instances, where the brachial plexus is involved in the malignant process, an interscapulothoracic amputation may be resorted to.

In still other cases where matastases of the viscera or other deep-seated metastases are present, the patient should be given all the relief and comfort that morphine and other analgesics will secure. Where nerve involvement exists, section of the posterior roots of the spinal nerves may afford relief of the pain; or in those desperate, but fortunately rare, cases where the spinal cord is invaded—the cases of paraplegia dolorosa—the suggestion made by Cushing of dividing the cord above the lesion may be humanely practised.

As before remarked, numerous operations for the radical cure of cancer of the breast have been devised and performed, but all of them partake of the essentials of the Halsted method. Many of these are characterized by ingenious flap-forming incisions. Warren's operation is among the most prominent of these, but it differs only slightly from that of Halsted, except that the dissection begins at the axilla and is carried on toward the sternum instead of in the reverse direction. In addition, Warren makes a plastic incision from the middle of the lateral margin of the wound and at right angles to it, and turns up a flap or flaps from the side of the thorax to cover in the denuded surface. Kocher's incision resembles a reversed figure of six, and is useful in many cases; Willy Meyer also employs a method that is quite popular; and Jabez N. Jackson has worked out an incision that is peculiarly applicable in fulfilling the requirements of the modern radical methods, together with supplying the necessary plastic flaps for reconstruction of the axilla and covering in the wound. J. B. Murphy has adopted a rather modified technique, the salient feature of which is the employment of muscle plastic procedures for the prevention of those disagreeable results that sometimes follow the extensive dissection, namely, fixation of the arm to the chest, with limitations of motion, venous stasis of the arm with edema (sometimes massive), persistent pain in the arm, and sensitive retracting cicatrices. To prevent these undesirable conditions he covers over and protects the axillary vessels with long and broad muscle flaps taken from the major pectoral and latissimus dorsi muscles. He does not remove the pectoralis major muscle, believing with Bryant of London, that in early cases the cancer cells do not penetrate beyond the fascia, and, consequently, does not hesitate to utilize this muscle for plastic purposes. Of course the latissimus muscle is usually free from the probability of infection. The arm is dressed in plaster at right angles to the chest. It seems probable that the functional disabilities as stated by Murphy are rather more pronounced than are generally encountered by the painstaking surgeon who gives careful attention to the axilla and its contained vessels. Mixter forms a large flap from the opposite side of the sternum, and slides over the sound breast to the midline or beyond it, by which means the wound surface is closed. Tansini describes an interesting procedure, which consists of two pear-shaped incisions, one on the front and the other on the back of the chest. The small end of the anterior ovoid cut tapers to a point in the center of the axilla, and the posterior ovoid incision slants outward from the axilla, being so curved as to form a broad base to the flap on a level with and reaching well back to the axilla. After the mamma has been cut away, the rear flap is pulled around to fill in the defect, and the long narrow triangle of skin which remains between the two ovoid incisions is drawn back and stitched in the denuded space behind. No contraction follows, and only an N-shaped scar remains.

In recent years Halsted has materially modified his original operation by removing a very much more extensive area of skin and gradually changing the shape of the incision to a large circular one surrounding the tumor, supplemented by a short vertical cut both above and below to facilitate dissection of the axilla. The margin of the axillary portion of the outer flap is stitched to the fascia immediately below the first rib so as to completely shut in the large vessels, and the remainder of the free edge of the skin, along the entire wound circumference, is sutured to the tissues of the chest wall. The widely denuded area is then covered over with large Thiersch grafts. In plastic operations the danger of necrosis of the flap is greater than it is with the grafts; and, furthermore, Halsted has noticed the important fact that the grafts offer a definite obstacle to the dissemination of carcinomatous metastases. He has observed cutaneous recurrences near the edges of the grafted area spreading rapidly and widely in the skin, but without involving the grafted portion except by encroachment at the margins. This observation has convinced him that the cases of extensive cutaneous dissemination, as seen in *carcinoma en cuirasse*, are probably not so hopeless as they were formerly considered, and that a much better chance for some of these unfortunates may be given them by

an enormous sacrifice of cutaneous tissue and supplying the defect with large skin grafts. He also suggests that in those instances of breast cancer showing a tendency to regionary cutaneous metastasis that the grafted space be encircled with a "moat" or gutter, by excising a narrow skin strip including its attached fat and loose fascia, and this to be filled in with grafts, with the reasonable expectation that by this means the cutaneous carcinomatous spreading may be confined within the limits of the space intervening between the grafted areas.

Of the many operative devices employed, the operations of Halsted, Warren, and Jabez Jackson, with minor modifications by different operators to suit individual conditions, are probably the more frequently used. Jackson's operation appears to offer certain advantages, especially the plastic feature, which enables the operator to carry out in a most thorough manner all the requirements of the modern procedure. The following description of this method, therefore, will serve as a fair type of the several steps of the complete modern operation.

Technique of Jackson's Operation.—The knife is entered in the depression or sulcus marking the interval between the deltoid and pectoralis major muscles, about one and a half inches below the middle of the clavicle, and is continued on in a straight line, parallel to the inner border of the deltoid, until it reaches the lower margin of the pectoral fold as it terminates in the arm. (Fig. 1133.) This linear incision is the only cut made at this time, the complete incision being omitted until the later stages of the operation, but if greater space is needed, a portion of the later incision that splits the pectoral fold may also be made. The incision thus made is deepened through the superficial fascia, exposing the fibers of the pectoralis major muscle as they converge to its tendinous insertion into the humerus. At the lower end of this cut, where it passes along the under margin of the major pectoral muscle, the index-finger of either hand is forced up beneath the muscle to emerge at its upper border, thereby hooking up the muscle on the finger, and by blunt dissection with the finger the muscle is separated out to the point of its insertion. (Fig. 1134.) If it is desired to leave the clavicular portion of the muscle (as advised by Charles Mayo), the finger is passed up through the well-marked sulcus between the clavicular and sternal bellies, and the clavicular belly excluded and left *in situ*. The tendon of the pectoralis, while lifted up on the finger, is next divided close to the humerus, and as the muscle is cut loose it retracts in an inward direction, leaving the lesser pectoral muscle exposed beneath and covered with its fascia. The finger is again employed as a blunt dissector, and is pushed on beneath this second muscle, freeing it as was done with the major pectoral, and then dividing the tendon at the point of insertion into the coracoid process. The muscle now retracts, and this retraction together with the separation of the wound by retractors fully exposes the axillary space from the front, allowing an easy dissection of this cavity. (Fig. 1135.) Thus far the bleeding has been insignificant, the vessels are in plain view, and all this has been accomplished without disturbing the breast in the least. The fascia surrounding the vessels is next opened on the outer side of, and parallel with, the vein by a cut with the scissors, and the fascia stripped from the vessels by gauze dissection and a few touches with the scissors or scalpel. The dissection is continued on from without inward toward the chest, clearing out fascia, fat, and glands, until the axillary vessels are completely isolated, and the vessels passing to the axilla and chest are plainly exposed. All the vessels requiring it are at once ligatured, which greatly limits the subsequent hemorrhage. After the axilla is cleared the original skin incision is completed as follows: "From the lower border of the first incision the knife is now carried along the under margin of the pectoral fold to the chest, at a point which corresponds, as a rule, with the lower border of the mamma itself. The remaining portion of the incision is made in the form of an ellipse about the nipple, with its long axis nearly vertical, or, rather, obliquely from above downward and outward to the outer quadrant of the breast. This ellipse is so planned as practically to make its outer curve parallel with the line of the first incision made, and thus to present, when completed, a quadrilateral flap with its base upward and entirely free below. This incision, of course, is carried through the skin and fascia down to the underlying muscular structures" (Jackson). Raising and turning upward toward the clavicle the elliptical flap gives a deeper exposure of the attachments of the pectoralis muscle above and in front. Each angle of this flap is caught with a tenaculum forceps, which facilitates its being fitted into place later on. The gauze dissection is now continued, loosening up the tissues beneath the pectoral muscles and the breast, toward the chest, and the pectoralis minor is then divided along its under surface close to the ribs and the costal muscles. The pectoralis major is then separated up to its clavicular and sternal attachments (at the same time dragging up the breast) which are cut from beneath. (Fig. 1136.) The perforating branches of the internal mammary artery are clamped when divided, as they emerge through the thoracic wall. The skin incision is next completed and the mass of muscles, fat, lymphatic glands, and breast, are removed in one unbroken whole. The quadrilateral flap of skin and superficial fascia which formed the anterior covering of the axilla are now stretched out by the tenaculum forceps holding the angles, and transplanted inward to fill in the defect of the chest wall left by the removal of the skin of the breast about the nipple, which is one of the special features of the Jackson operation. (Fig. 1137.) The margin of the lower portion of the pectoral cutaneous fold, which represents the area of skin that formed the original floor of the axilla, is grasped with forceps and pulled up to the point of beginning of the first incision beneath the clavicle, which snugly covers in the axillary vessels and obliterates, anatomically, the axillary cavity. The flaps are sutured with silkworm-gut threads, continuous or interrupted, and drainage is provided for by a stab wound behind in the most dependent position. (Fig. 1138.) A voluminous antiseptic gauze dressing completes the technique.

Jackson claims for his method these advantages: The plastic flap entirely covers in the wound space without tension; the drawing of the skin up to the arm obliterates the axilla at once which prevents the usual scar tissue and subsequent pressure on the axillary vessels and nerves; the ligation of all vessels near their origin lessens the hemorrhage, together with the number of attached hemostatic forceps which are obstacles to quick work; and, finally, the most difficult and important steps of the procedure are completed before the breast is removed, thereby diminishing shock incident to prolonged exposure of the large chest wound.

The After-treatment.—The dressing of the arm and the treatment of the patient after operation are of much importance. Stiffness and atrophy of the parts, thus interfering with the function of the arm, is one of the disabilities to be especially feared, and hence arm and shoulder massage together with passive movements should be commenced within the first ten or twelve days and continued for several weeks. By these measures a useful member is obtained, and with surprisingly little curtailment in the shoulder movements. Fixing the arm at right angles to the chest by plaster, by various models of splints, and other devices have been employed for the same purpose by different surgeons. Ewald uses a simple method, which is carried out by drawing up and fixing the hand and arm above the patient's head, by means of a wooden peg and

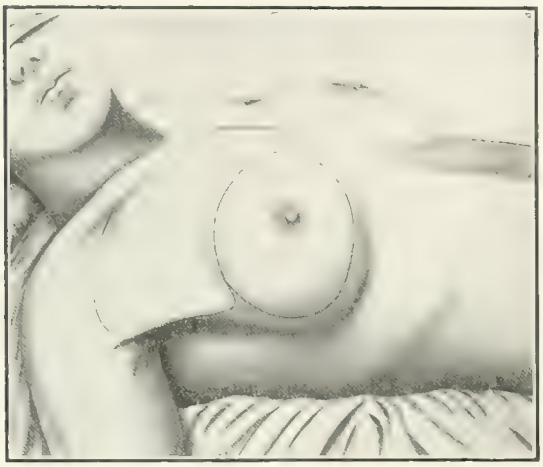

FIG. 1133

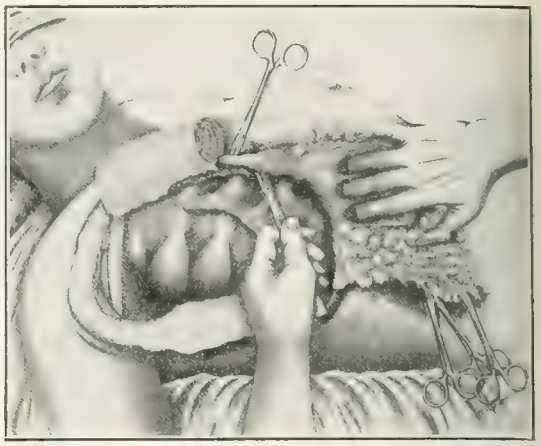

FIG. 1136

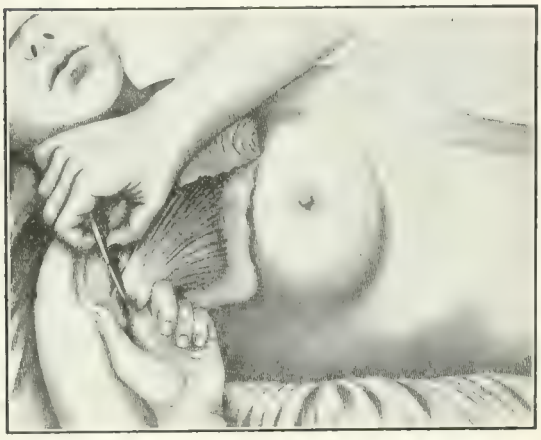

FIG. 1134.

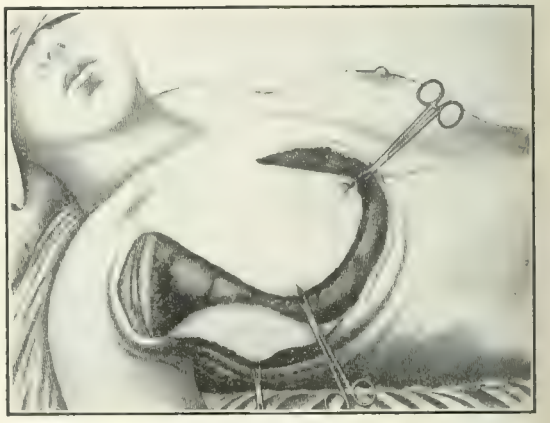

FIG. 1137.

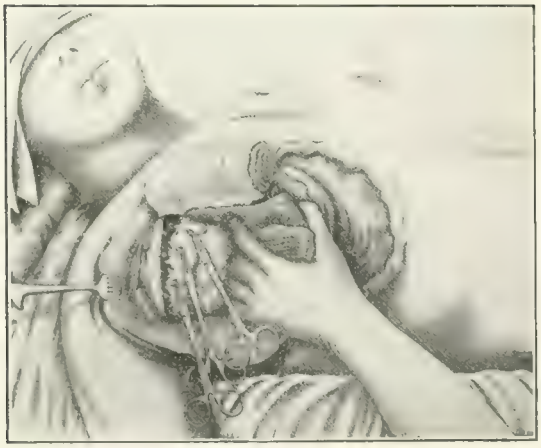

FIG. 1135.

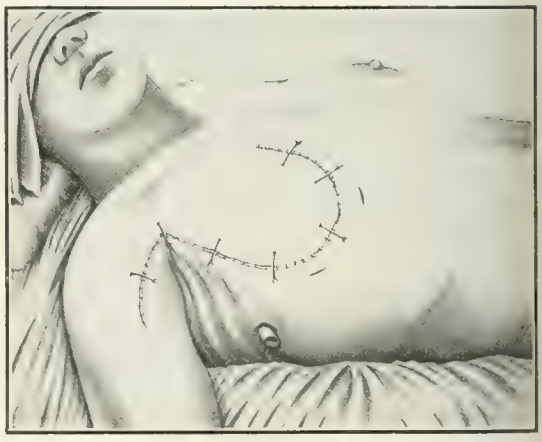

FIG. 1138.

FIGS. 1133 to 1138.—Illustrating the Several Steps in Jackson's Operation for Complete Amputation of the Breast. (After J. N. Jackson, Jour. Am. Med. Ass'n., January 15, 1910.)

bandages fastened, on the principle of a sling, to a horizontal support extending at a right angle from an upright rod attached to the head of the bed. A sling around the elbow gives additional support to the arm.

The patient should be gotten out of bed as early as is consistent with safety, that is in about seven to eight days on an average. Earlier than this may cause dislodgment of a thrombus, and a fatal termination may follow. Warren reports such an accident with death in one of his cases. The patient should, if possible, be kept under observation at intervals for several years, in order that early recognition and prompt excision of any local recurrence can be performed.

Sarcoma.—Sarcoma is one of the very rare diseases of the breast, being proportionately much less common than in other organs and localities of the body, which is a matter of some surprise when the histology and structural changes of the gland are considered. The frequency of sarcoma is variously estimated. Roger Williams found ninety-four cases in 2,397 breast neoplasms, or 3.9 per cent.; at a later date Rodman in an analysis of 5,000 cases, principally taken from German clinics, estimated the proportion at 2.7 per cent.; and Bloodgood encountered fourteen instances in 694 cases, a percentage of only 1.5, in the Johns Hopkins Hospital. These figures, especially those derived from the last two, and probably the more reliable, series, indicate the rarity of the affection.

Sarcoma belongs comparatively to the young breast. It may occur in early childhood but is rare before puberty, and seems to invade the gland preferably between the third and fourth decades, that is, during the period of physiological activity of the gland. It is infrequent after the cessation of menstrual life, thereby differing from carcinoma. In sixty cases collected by S. W. Gross only thirteen were in individuals over forty years of age. No direct association between the disease and either the sterile or the child-bearing state is traceable. Traumatism is claimed to be a causative factor, and in certain instances seems to bear such a relationship; but antecedent inflammatory processes have not been shown to have any etiological connection with the disease.

A few instances of sarcoma have been met with in the male breast. These cases were of the primary form, and a number of them originated in moles on the skin of the mamma. No case of secondary origin has been observed. All the histological types were found, but the spindle-celled variety largely predominated. Williams found three cases in a series of twenty-five tumors; Finsterer, in 1906, collected twelve cases from the literature; and in 1907 Connell reported a personal case and, at the same time, presented a group of thirty-four cases he had succeeded in collecting. Heredity and traumatism seem to assume a rôle of less importance than in carcinoma. Sarcoma also appears at an earlier average age than does carcinoma.

Mammary sarcoma may be *primary* or *secondary*. The primary forms are derived from the connective-tissue elements of the gland—resembling those in the embryonal or transitional stages—and arise either from the intralobular hyaline connective tissue or from the more dense interstitial fibrous stroma which surrounds the glandular lobules. The secondary form is extremely rare and develops from a preexisting or primary focus elsewhere in the body—sarcoma of the ovary and tonsil, for example, being responsible for such metastases. All the several cellular types may exist in the breast, but the spindle-cell variety is oftener seen, the round cell comes next, and the giant cell and the melanotic types are extremely rare.

The variety arising from the hyaline connective tissue surrounding the smaller ducts and acini, spoken of as the cystic form, is much the more common, and is said to represent eighty per cent. of the sarcomatous and two to three per cent. of all malignant diseases of the mamma (Finney). It has a common origin with the fibroma, and is apparently a late stage of intracanalicular myxoma. Indeed, Bloodgood states that he has observed only two cases of sarcoma of the breast that did not originate in large intracanalicular myxomatous tumors, although he has never seen it in small growths of this character. In the second form, the so-called solid sarcoma, the neoplasm develops from the interstitial connective tissue of the gland, and pushes aside and compresses the glandular elements.

Pathology.—The tumor is apparently distinctly encapsulated, the capsule being composed of connective tissue displaced by the increasing growth. The surface of a fresh section is flesh color and has much of the appearance of the fibroma, although the clefts are larger and the connective tissue more prolific, and the polypoid growths crowd into the clefts and slits and rise up over the cut surface. There is some epithelial growth, as shown by the cells piled up in several rows and even filling the cysts, but for the most part the epithelium has disappeared from the surface of the clefts, having exfoliated and become mixed with the mucus filling the cyst cavities. Occasionally blood may fill the spaces, but usually they are empty. The structure may be composed of spindle cells or round cells, and this may vary in different portions of the same growth. Thus, in some parts the structure is fibrous, in some parts sarcomatous tissue exists, and in other parts myxomatous structure is to be seen. Calcareous degeneration, cartilaginous deposits, or even osseous material is sometimes found in ancient growths.

Symptoms and Clinical Course.—Commonly the tumor is located centrally and beneath the nipple, but when it is seated in the periphery of the gland it evinces a predilection for the inner and upper quadrant. The growth is ordinarily single and unilateral, but both breasts may be affected, and the tumors may be multiple. At first it is encapsulated, easily moved about, and the adjacent structures seem to be unaffected; but the capsule does not always shut it off from the surrounding structures so as to prevent extension, as shown in the occasional occurrence of early metastasis. Pain and tenderness are not prominent, but may appear at the menses; the nipple is not retracted and the skin is unimplicated. The small growths are firm, of a somewhat irregular outline, and nodulated. In cases of long standing the process involves the whole gland together with the nipple, and may even involve the pectoral fascia and muscle. As the tumor grows it assumes an irregular shape, with bosses or protuberances; the occurrence of cysts is common, and hemorrhage into these cysts may produce a marked and sudden increase in size, and a change in the contour of the tumor. The skin become red, adheres to the mass, and later may ulcerate, to be followed by the out-cropping of a foul smelling fungous mass. The edges of the ulcerated skin are not adherent or thickened, but sharply margined. Large veins course over the surface, and a discharge from the nipple may or may not exist. The axillary lymph nodes may now enlarge but this is not usual, and when present is due to inflammatory hyperplasia and rarely to metastasis. Metastatic deposits are more common in the viscera and skin, and evince decided preference for the lungs. Metastasis or generalization (sarcomatosis) occurs by way of the blood-vessels and not ordinarily by the lymphatic route, which accounts for the usual immunity to infection of the axillary lymph nodes. This also explains the frequent occurrence of secondary growths in the pulmonary areas, since the lungs present the system of capillaries in nearest proximity to the breast, and in which locality embolic sarcoma cells, swept on by the blood stream, are more apt to be lodged. Metastases may occur early and when the tumor is small, therefore, the lungs should be carefully examined to determine the possible

presence of a secondary growth, before operation is decided upon. Intercurrent inflammations are apt to give impetus to the progress of the disease; and when the tumor develops during pregnancy or lactation its growth increases with extreme rapidity, and the disease has a promptly fatal termination. Elevated temperature, both local and general, has been noted in rapidly growing tumors.

Diagnosis.—These tumors are always benign in the beginning. Therefore in the early stages the diagnosis is a matter of extreme uncertainty, and, more frequently than otherwise, cannot be made until after excision and microscopic examination. The chief clinical features of sarcoma are its irregular and comparatively slow growth, the large proportion it reaches, its distinct capsule, in the early stages its resemblance to fibroma, and the absence of lymphatic infection. Having a common origin, as it were, with the fibroma, it is difficult to differentiate it from that neoplasm, and especially from the intracanalicular myxomatous type. It may be mistaken for a cyst, and it has many symptoms in common with medullary carcinoma. The appearance of the tumor, its location, whether single or multiple, the existence of softened or fluctuating spots, and the absence of glandular infection, taken together should offer a group of symptoms suggestive of sarcoma. In the late stages the diagnosis is much less difficult, excluding the probable confusion with the medullary form of carcinoma.

Prognosis.—Both metastasis and local recurrence are frequent in sarcoma of the breast. In large tumors and at a late stage of the disease recurrence is very common, and S. W. Gross, whose figures are evidently based upon these advanced types, states that such occurs in more than fifty per cent. of the cystic forms. But in the early stages the tendency to recurrence after operation is decidedly less. The more recent statistics of Poulson show that in seventy-five per cent. of breast sarcomata there was no recurrence at the expiration of five years, and he regards the end results as more favorable than in carcinoma. It has been noted that the softer and rapidly growing tumors are more prone to recurrence, as contrasted with the harder and less active growths. Sarcomata of the breast display a greater degree of malignancy in young than in more elderly individuals. Again when occurring in the declining stage of the mammary gland it evinces less tendency to local recurrence but a greater disposition to metastasis or generalization; whereas in the gland that is in a state of functional activity the reverse obtains, greater recurrences and fewer metastases. In the round celled variety the prognosis is less favorable than in the tumor composed of spindle cells, although in the latter a remarkable disposition to local recurrence has been noted. The melanotic type is extremely malignant.

It has been demonstrated that prompt and repeated operation for recurrences may result in permanent recovery, as illustrated by the well-known case of S. D. Gross to be referred to later; and Warren states that the patient may be regarded as safe if there is no recurrence for four years after the last operation.

Treatment.—Sarcoma does not admit of concession or temporization in its treatment, but in the large majority of instances calls for prompt and complete removal of the breast including the pectoral muscles. This is the only safe procedure in every case, and is imperative in large and rapidly growing tumors. It is often stated that at an early stage and in small growths, removal of the tumor along with a wide area of healthy gland structure—outside of all infiltration—is sufficient; but complete excision of the breast in all cases seems to be the wiser course. After invasion of the axillary lymph nodes, a cure is not probable. But even then permanent relief is occasionally secured; besides, radical procedure may hold the disease in abeyance for a time, and therefore, when practicable, the patient should be given the benefit of operation. When generalization of the disease has taken place, surgery is useless.

Where the case is inoperable and recurrent, injection of Coley's toxins into the tumor deserves consistent trial, and in some instance has been followed by decided shrinkage of the growth and a seeming cure. In the same class of cases the Roentgen ray may be tried, although it offers but scant prospect of success.

Local recurrences should be promptly dealt with, and even after repeated operations a final cure may result. S. D. Gross reports the remarkable case of a single woman upon whom twenty-two operations were done, removing fifty-one recurrent growths in four years—sacrificing a large portion of the pectoral and other costal muscles—and who was in perfect health nearly eleven years after the last operation.

William McDowell Mastin.

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Breath.—The respired air, from A. S. brâed, breath, odor. Skeats suggests that it may be allied to Latin *fragrare*, to emit a scent: *fragum*, a strawberry; but this is uncertain. Thus in the very origin of the word there is inherent the idea of odor. The breath consists of nitrogen and oxygen, the proportion of the latter being less than that present in the atmosphere; a little more than four per cent. of carbonic acid, aqueous vapor, ammonia, and organic impurities. In recent years much work has been done in investigating the nature of the organic matter of expired air. Ben obtained 100 c.c. of water from 3,000 liters of expired air. The odor of this water was peculiar but not disagreeable. Its organic contents weighed five milligrams. There were no alkaloids in it, but it gave a reaction for ammonia. There is no certain knowledge as to whether microorganisms may be eliminated by the breath, although the laity believe in this possibility. Welch states that the consensus of authority is against the probability of such an occurrence. Experiments have shown the difficulty with which microorganisms are detached from moist surfaces by air currents, so that it is likely that they are never conveyed to the outside air by ordinary quiet breathing. The proportion of carbonic acid is increased in the early stages of smallpox, measles, and scarlatina, and during the existence of any extensive skin disease. It is diminished in typhus fever. The temperature varies somewhat, being influenced slightly by that of the external air, but seldom falls below 90° F. When the temperature of the inspired air is very high, as in the hot room of a Turkish bath, the breath may appear, by comparison, to be cool. In fevers its heat is increased, but in the algid stage of cholera it is almost cold.

In health the breath is nearly odorless, but there is a sweet odor from certain glands at the mucocutaneous junction of the nostrils. Nature has designed this as a sexual excitor, and together with other attractions between the sexes it helps to insure reproduction of the species. This is not characteristic alone of the female, but the male also, if living a comparatively normal life, possesses the same attraction. The pleasure of kissing is due chiefly to this source. Consequently, in blunted olfactories, osculation loses its greatest charm. Each person is characterized by his own peculiar nasal odor, and the more refined he is, and the higher in the scale of civilization, the more delicate the odor. On the contrary, the coarser the individual, the more heavy the odor, *e.g.* negroes emit a musky odor. Indi-

viduals who are not in good condition for reproduction, or who are lacking in passion, possess slight nasal odors. It has been stated to be absent or disagreeable in pregnant women.

Among the curiosities of literature, there are reported cases of luminous or bright red breath; and others of inflammable breath—in which there was a flash of flame from holding a lighted match near the mouth. This last phenomenon is probably due to the formation of combustible carbureted hydrogen from the chemical decomposition of breath. James Gray, in the *Lancet*, speaks of the "peculiar odor of the breath previous to death," and cites two cases in which was exhaled the same phosphoric odor just before death.

The odor of the breath is modified temporarily by many causes. Mental emotion often exerts a powerful influence over it. If the many well-known pathological effects of excessive emotion be reviewed, this fact will not seem strange. For mental disturbance may so change the secretions of the alimentary tract and the glandular system that the normal elimination of waste products is prevented, and an extra burden is thrown on the lungs, with resulting foul breath. Or the sudden excitement may cause a greater destruction of tissue than normal, so that before the intestinal glands can accommodate themselves to this increase the burden of vicarious elimination is thrown upon the lungs. The subjects are not always conscious of its presence. There is generally a pasty taste in the mouth, and this together with the disagreeable breath may be almost instantaneous with the occurrence of the emotion. Such patients are commonly neurotic and high-strung and possess a mercurial temperament. Many volatile substances taken into the system through the ordinary channels are excreted in part through the lungs, and impart their odor to the breath. Thus turpentine, alcohol, onions, cheese, spices, and many other alimentary and medicinal substances taken into the stomach are quickly detected by their peculiar smell in the expired air. In women the expired air frequently acquires a disagreeable character during the menstrual period, said to be due to the nasal and retronasal secretion of the mucous membrane, which at that time is congested. In feverish conditions the breath acquires a sweetish, or sometimes sickening, character. This is particularly noticeable in children, and in them is often suggestive of the odor of chloroform. In diabetes mellitus there is often a peculiar sweetish odor, which is difficult to describe, and which has been likened to that of honey, sweet apples, or hay. In uremia the breath is said often to acquire a strongly ammoniacal odor due to the non-elimination of the urea, which persists in the blood and combines with the water to form carbonate of ammonium. The skin also exhales the same odor. In pyemia also the breath is peculiar and characteristic. Dr. Tavignot, a French writer, described, some years ago, a peculiarity of the breath in glaucoma, to which he gave the name of *haleine safranée;* and he maintained that this was constantly present in persons suffering from that affection. There are cases recorded of extensive burns in which the breath, formerly sweet, has assumed the disgusting odor of bisulphide of carbon. Migraine may be accompanied by a bad breath. Tuberculosis can often be detected by a characteristic breath. Pernicious anemia, pseudoleucemia, and interstitial nephritis also frequently have this symptom.

Various mineral substances, which are themselves nearly or quite without smell, cause, when introduced into the system in sufficient quantities and during a certain period of time, a very disagreeable odor of the breath. This occurs from stomatitis in some cases, and in others from the disturbance of digestion, induced by the chronic poisoning. The substances which most frequently are concerned in the production of toxic halitosis are: antimony, arsenic, lead, mercury, phosphorus, and sulphur. Sulphur imparts a distinct odor after two hours, not only to the breath, but also to the perspiration.

In chronic alcoholism the odor of the expired air is very foul, not necessarily alcoholic unless liquor has been recently taken, but possessing a peculiarity all its own, and unlike anything else. The excessive use of tobacco not infrequently imparts a foul odor to the breath.

A permanent foulness of the breath is due either to interference with the elimination of the products of decomposition by the intestines and kidneys or to local causes existing in some part of the respiratory tract.

Perhaps the most frequent cause of a bad breath is dyspepsia, either gastric or intestinal. The hurry, excitement, and worry characteristic of our present century are greatly to blame for these ills. Overwork, excessive application to business, sedentary habits, and the habit of "bolting" food, all bring in their train disastrous results. In this case the elimination of the products of decomposition and of the effete matters of the tissues by the normal channels is interfered with to a greater or lesser extent, and the task of their excretion from the economy is in part thrown upon the lungs. The expired air contains a large amount of organic matter, which is often very ill-smelling and offensive. In cancer of the stomach or liver, disordered digestion is often heralded by a foul breath. In chronic constipation, especially, the odor of decomposing organic matter is most marked. A very common symptom of intestinal worms, especially ascarides in children, is foul breath.

Among local causes there are various affections of the mouth, nose, pharynx, larynx, and lungs.

Many cases of foul breath are due to layers of thickened and decomposing epithelium commonly covering the upper surface of the tongue, especially at the base of this organ. These masses may be scraped from the surface by means of a tongue depressor or spatula.

Dental caries is a well-known cause of foul breath. This arises not only in consequence of the decay of the teeth, but also, and chiefly, from decomposition of food lodged in the cavities and between the teeth. These causes may give occasion to a fetid breath in persons who are careless in cleansing the mouth, even when the teeth are perfectly sound. Gingivitis, from arsenical or mercurial poisoning, or from scurvy, may give rise to a bad breath, as may also syphilitic ulcerations of the buccal cavity or fauces. Pyorrhea alveolaris is also another cause. "Spontaneous stomatitis" occurs without any apparent cause. The entire interior of the mouth is affected, and the fetid saliva taints the breath. In many points this affection resembles mercurial stomatitis. Follicular stomatitis occurs at any age. This inflammation takes its origin in the follicles of the mucosa, on the inside of the lips, and on the sides of the tongue. In certain cases a vesicular eruption (herpes) is the first manifestation of the disease. There is a condition known as catarrh of the tongue, which is usually associated with dyspepsia, but may occur independently of it. Here again decomposition of mucus, epithelial scales, and food particles as well as bacteria are the offending cause. In necrosis of the jaw which may result from mineral poisons, decayed teeth, or syphilis, the odor is frequently sickening. The breath of patients suffering with carcinoma of the tongue and neighboring parts is very penetrating, but that from cancrum oris is almost unbearable, and once experienced can never be forgotten.

In nasal polypi, after the secretion from the nose becomes mucopurulent, the breath is apt to be disagreeable. Ozena, from whatever cause produced, is frequently responsible for a most foul and repulsive odor. This is due, according to Browne, to the fact that "the crusts and discharges usually contain decomposing fatty globules and microorganisms."

Mouth-breathers with nasal stenosis are often afflicted with bad breath.

Like the odor of necrosis of the jaw, that of follicular tonsillitis and pharyngitis is sickening. In the latter case the odor is due to decomposition of the secretion and food particles filling up the follicles, and is often suggestive of fecal matters. This inspissated secretion becomes cheesy in consistence. Chronic enlargement of the tonsils is apt to occur in young people with the so-called scrofulous diathesis. The breath in these cases is often foul. In diphtheria there may be a disagreeable fetor of the expired air suggestive of putrefaction. Putrid sore throat shares with diphtheria this symptom of halitosis. Syphilitic and tuberculous ulcerations in the larynx often impart an unpleasant odor to the breath, and the fetor of some forms of bronchitis, of bronchiectasis, and of abscess and gangrene of the lungs is too well known to require any description.

Finally, some individuals suffer from a more or less fetid breath, the cause of which it is impossible to discover. It is often congenital; it is constant, and not dependent upon any apparent deviation from health, but may be associated with a strong and unpleasant odor of the sweat and other secretions.

In the following table the various conditions leading to the production of a bad breath are arranged under their several classes for convenience of reference.

Causes of Halitosis.

Transient	Mental disturbance.
	Various ingesta, medicinal and alimentary.
	The menstrual period.
Systemic	Fevers.
	Diabetes mellitus.
	Uremia.
	Pyemia.
	Glaucoma (?).
	Burns.
	Migraine.
	Tuberculosis.
	Pernicious anemia.
	Pseudoleucemia.
	Interstitial nephritis.
Toxic	Antimony.
	Arsenic.
	Lead.
	Mercury.
	Phosphorus.
	Sulphur.
	Alcohol.
	Tobacco.
Digestive	Gastritis.
	Dyspepsia.
	Cancer of stomach or liver.
	Constipation.
	Hepatic disorders.
	Enteritis.
	Intestinal worms, particularly ascarides in children.
	Dental caries.
Buccal	Gingivitis.
	Stomatitis.
	Pyorrhea alveolaris.
	Lingual catarrh.
	Necrosis of jaw.
	Carcinoma of tongue and other parts.
	Cancrum oris.
	Lack of cleanliness.
Nasal	Polypi.
	Ozena.
Faucial	Follicular tonsillitis.
	Follicular pharyngitis.
	Syphilitic ulceration.
	Diphtheria.
	Putrid sore throat.
Laryngeal	Carcinoma.
	Ulceration.
Pulmonary	Bronchiectasis.
	Putrid bronchitis.
	Tuberculous ulceration (cavities).
	Gangrene.
	Abscess.
	Carcinoma.
Idiopathic.	

The treatment of a foul breath consists essentially in discovering, and, if possible, removing the cause. In by far the largest number of cases the origin of the trouble resides in digestive disturbances, usually associated with constipation, or in carious or dirty teeth. The first care of the physician should be, therefore, to regulate the digestive functions, and to see that the hygiene of the mouth is properly attended to. If the gums are spongy or receding, a tooth wash containing myrrh should be used. All cavities should be plugged with gold or some other suitable filling, as the dentist may advise, and the tartar, which accumulates between and behind the teeth, should be removed from time to time. The teeth should be picked after each meal to remove the particles of food, or, better still, they should be cleaned by means of dental floss, and should then be brushed with plain water, soap and water, or a reliable dentifrice. If the stomach is at fault, in addition to the remedies suitable to the condition, a piece of charcoal cake or charcoal powders may be taken shortly after meals. An odor which cannot be removed may be more or less effectually disguised by oil of nutmeg, cinnamon, cardamom seed, cloves, pimenta, lavender water, sweet-flag, leaves of the common partridge berry, allspice, coffee, or other aromatics. A solution of carbolic acid (1 to 200) may be used as a mouth wash or gargle when the fetor is due to organic destruction of tissue. The following is an agreeable mouth wash which will often disguise unpleasant odors: Thymol, 0.50 gram (7½ grains); alcohol, sixty-two grams (two ounces); borax, one gram (fifteen grains); distilled water, 500 grams (one pint). The mouth is to be rinsed frequently with this solution.

For persistent foul breath, Howe advises the following combination. In the first place, the teeth should be thoroughly cleansed and the gums sponged with a solution of myrrh and water; then one of the following lozenges may be allowed to dissolve in the mouth: Powdered cinnamon, pimenta, and cardamom, of each two grams (thirty grains); white sugar, four grams (one drachm); mucilage of gum acacia, q.s. to make fifty troches.

In conjunction with these, the following may be employed: Powdered caraway seed, coriander seed, and cinnamon, of each two grams (thirty grains); white sugar four grams (one drachm), mucilage of gum acacia, q. s.; make fifty troches. Dissolve one in the mouth when necessary.

All these deodorizers are, however, of necessity merely palliative in their effects, and the cause should always, if possible, be searched for and removed.

Emma E. Walker.

Brehmer, Hermann.—Born in Kurtsch, Germany, on August 14, 1826. He received the degree of Doctor of Medicine from the University of Berlin in 1853. In 1854 he established at Goerbersdorf an institution which had for its object the cure (largely by an outdoor life) of pulmonary consumption; and from that time to the end of his life he devoted all his energies to the efficient management of this institution. As soon as its success became known it served as the model for many similar establishments in various parts of the world; it was also the forerunner of those high-altitude resorts the importance of which in the treatment of pulmonary tuberculosis is to-day being more and more thoroughly recognized. Brehmer died on December 23, 1889. (Pagel.)

Schuchardt of Gotha has written a very full account of Brehmer's life and of the manner in which he conducted his institution at Goerbersdorf. This article will be found in the "Jahrbuch der Königl. Akad. gemeinnütziger Wissenschaften zu Erfurt," Neue Folge, Heft xxiv., 1898; its title is: "Zur Geschichte der Anwendung des Höhenklimas

(Gebirgsklimas) behufs Heilung der Lungenschwindsucht (Lungentuberculose)." A. H. B.

Bretonneau, Pierre.—Born at Saint-Georges-sur-Cher, France, April 3, 1778. About 1798 he came to Paris and began the study of medicine. Failing, however, at the proper time to pass the examinations necessary for obtaining the degree of Doctor of Medicine, he returned to Tours and began the practice of his profession under the simple title of "Officier de Santé." Thanks to an epidemic of typhoid fever which prevailed in the Touraine from 1816 to 1819, he had the opportunity to learn a good deal about the pathological anatomy of this disease. It was he who first noted the existence of an eruption on the intestinal

Fig. 1139.—Pierre Bretonneau.

mucous membrane, and he then gave to the disease the name of "dothienentérite." A few years later his pupil, Armand Trousseau, described the lesions more minutely. From 1818 to 1821 the Touraine was visited by a second epidemic of disease of a serious nature. From the external appearance presented by its characteristic lesion Bretonneau gave to this disease the name of "diphthérite"—a name which has since become firmly fixed in medical nomenclature. The latter discovery will be found described in an article published by him in 1826 under the title: "Des inflammations spéciales du tissu muqueux, et en particulier de la diphthérite, ou inflammation pelliculaire, connue sous le nom de croup, d'angine maligne, d'angine gangréneuse," etc. He died at Passy, a suburb of Paris, on February 18, 1862. (Pagel.)

It is not entirely due to the two discoveries mentioned above that Bretonneau has found a place in the history of medicine, for he was one of the most original characters imaginable, even in his ordinary everyday life. A. H. B.

Brides-Les-Bains is a spa in Savoy, France, often called, because of the composition of its waters, the French Carlsbad. Until recently the place was practically inaccessible, the nearest railway station being twenty miles away. Now, however, the railroad has been extended and there is a station at Moûtiers, distant only three miles. The village is most picturesquely situated, at an altitude of 1,800 feet above sea level, in a valley running from southeast to northwest, enclosed on either side by almost precipitous mountain slopes.

Access.—The station of Moûtiers is on the Paris, Lyons, Mediterranean Railway, 672 miles, or thirteen hours, from Paris; fare, 75 fr. 35 c. first class, and 50 fr. 90 c. second class.

Analysis.—The following is the composition of the water, according to an analysis made by Willm in 1890:

	Grams, per liter.	Grains, per pint.
Carbonate of calcium	0.3133	2.7752
Carbonate of magnesium	.0112	.0992
Carbonate of iron	.0078	.0692
Silica	.0464	.4108
Chloride of sodium	1.8318	16.2244
Sulphate of sodium	1.1604	10.2836
Sulphate of potassium	.0946	.8380
Sulphate of lithium	.0095	.0840
Sulphate of calcium	1.7143	15.1940
Sulphate of magnesium	.5288	4.6836
Arsenate of sodium	.0008	.0071
Phosphates, bromides, iodides	Traces.	Traces.
Carbonic acid forming bicarbonates	.2934	2.6012
Free carbonic acid	.1017	.9008

Indications.—The waters of Brides are in moderate doses laxative, in larger quantities (six to eight glasses daily) purgative. It is claimed that they can be taken for many days in succession without increasing the dose, and they do not irritate to the same degree as do many of the stronger purgative waters. They are used in various disorders of the abdominal viscera, such as congestion of the liver following dietetic imprudences or alcoholic excesses or a prolonged residence in the tropics, gallstones, constipation, functional disturbances of the digestive tract, obesity, the so-called uric-acid diathesis, gravel, diabetes, anemia and chlorosis, and chronic congestion of the uterus and adnexa. In many cases treatment with Brides water internally is combined with baths at Salins-Moûtiers, distant two miles from Brides.

Accommodations.—There are four hotels at Brides, in addition to numerous boarding houses, which afford good and ample accommodations at from six to eight francs and upward a day. A casino, music in the park, and the usual attractions of the continental spa are to be found here. There are two churches, a Catholic and a Protestant, the latter being served by an English clergyman during the season. The climate is mild, but not enervating. The season extends from the middle of May to the middle of September.

Salin-Moûtiers.—This is a small thermal station in Savoy, France, distant 672 miles from Paris, on the Paris, Lyons, Mediterranean Railway. It is situated in a narrow valley in a grandly picturesque country, at an elevation of about 1,500 feet above the level of the sea. It is two miles from Brides-les-Bains, with which it is connected by an electric railway.

Analysis.—The following is the composition of the water, according to an analysis made by M. Willm, Professor of Chemistry at Lille, in 1890:

	Grams. per liter.	Grains. per pint.
Carbonate of calcium	0.6488	5.8392
Carbonate of magnesium	.0089	.0801
Carbonate of iron	.0136	.1224
Silica	.0332	.2988
Chloride of sodium	12.4886	112.3974
Chloride of potassium	.1695	1.5255
Sulphate of lithium	.0046	.0414
Sulphate of calcium	2.0638	18.5742
Sulphate of magnesium	.8460	7.6140
Arsenate of sodium	.0007	.0063
Phosphates, bromides, iodides	Traces.	Traces.
Organic matters and losses	.0192	.1728
Carbonic acid forming bicarbonates	.5906	5.3154
Free carbonic acid	.3854	3.3486

Indications.—The waters of Salins-Moûtiers are employed chiefly for bathing, usually in connection with

the internal use of the water of Brides-les-Bains, but they are also taken internally in special cases. Accordingly to D. W. Samways, "for young people with enlarged glands, anemia, chlorosis, or general lack of vigor, these baths are excellent, especially in conjunction with the climatic advantages of the locality. For the overworked or neurasthenic, for those also in whom convalescence is tardy, they are similarly very reviving. For such cardiac affections as can be relieved or controlled by baths and exercises similar to those in vogue at Nauheim, and for certain congestions and disorders of the uterus and its appendages they are also very beneficial."

Accommodations.—There is a hotel at Salins-Moûtiers, and there are also many boarding houses in the village where guests may find suitable accommodations. Most of those who take the baths, however, do so in conjunction with the internal use of the waters of Brides-les-Bains, and live at the latter place. The climate is mild but invigorating. The season lasts from the middle of May to the middle of September.

EDWARD O. OTIS.

Briggs, William.—Born at Norwich, England, in 1641. He obtained his academic training at the University of Cambridge, and then went to Montpellier, France, where he pursued his medical studies under Vieussens. In 1676, after he had returned to England, he published his treatise on the anatomy and diseases of the eye. In 1677 Cambridge University conferred on him the degree of Doctor of Medicine, and soon afterward he was made a member of the Royal Society of London. In 1683 he was appointed an attending physician at St. Thomas' Hospital, and a few years later was chosen by King William to be his Physician-in-Ordinary. He died September 4, 1704, at West Malling in the County of Kent.

Briggs was chiefly distinguished for the researches which he made into the anatomy of the eye and for the extensive knowledge which he acquired of the diseases of this organ. The great Newton held him in high esteem. The book to which reference has already been made bears the following title: "Ophthalmographia, sive oculi ejusque partium descriptio anatomica," Cambridge, 1676. In the edition which was published at London in 1685, the author furnishes a new theory of vision. Briggs is said to have been the first anatomist to show clearly the relations between the optic nerve and the retina.

A. H. B.

Briggs, William Thompson.—Born, December 4, 1828, at Bowling Green, Kentucky. He received the degree of Doctor of Medicine from the Transylvania University in 1849. In 1851 he established himself in Nashville, Tenn. For several years he held the position of Professor of Surgery in the Vanderbilt University of Tennessee. His death occurred on June 13, 1894.

Among the more important publications which attest his wide experience and his skill as a surgeon, the following deserve special mention: "History of Surgery in Middle Tennessee"; "Traumatic Aneurysm of the Internal Carotid, the Result of a Puncture, Ligation of the Common Carotid and then of the Internal Carotid at the Seat of Injury"; "Trephining in Epilepsy." A. H. B.

Bright, Richard.—Born in Bristol, England, September 28, 1789. He began the study of medicine in 1809 at the University of Edinburgh. In 1810 he accompanied Sir George Mackenzie and Sir Henry Holland on a voyage to Iceland. In the book which the former afterward wrote about this trip ("Travels in Iceland") Bright contributed the part relating to the natural history of the region. In 1811 and 1812 he frequented Guy's Hospital, London, and in 1813 he received the degree of Doctor of Medicine from the University of Edinburgh. In 1814 he made a prolonged trip through Germany and Austria for scientific purposes, and published the results in a book entitled: "Travels from Vienna through Lower Hungary," etc. (Edinburgh, 1818). From 1817 to 1820 he was assistant physician in the Fever Hospital, London; and, after acting for four years as assistant physician, he

Fig. 1140.—Richard Bright.

was made (in 1824) full physician of Guy's Hospital. His connection with the latter institution continued up to the time of his death, which occurred on December 16, 1858.

Bright, in his lectures, paid a great deal of attention to pathological anatomy. The more important details regarding the discoveries which he made in the pathology of the kidneys will be found in the "Reports of Medical Cases selected with a View to Illustrate the Symptoms and Cure of Diseases by a Reference to Morbid Anatomy" (2 vols., London, 1827 and 1831). The publication of the first of these volumes marks an epoch in the history of medicine; and, as a result of his discoveries. Bright's name has been permanently attached to diseases of the kidney. Then, besides, he was one of the first to describe the conditions known as "yellow atrophy of the liver" and as "pigmentation of the brain" in miasmatic melanemia, etc. In 1837, when Queen Victoria mounted the throne, Bright was appointed her physician extraordinary. A. H. B.

Bright's Disease.—See *Kidneys, Diseases of.*

Brill's Disease.—The significance of this newly described syndrome depends chiefly on the question of its identity or non-identity with exanthematous typhus. Should it prove to be only an aberrant type of the latter, its consideration would belong purely under that head. If the balance of evidence is in favor of its autonomy, it naturally merits a full independent discussion, just as does the so-called "fourth disease" of Dukes, when contrasted with measles, rötheln, and scarlet fever. Indeed, Brill's disease might well be termed the "third disease" in a group orginally made up of typhus and typhoid (paratyphoid).

Brill's outline of his symptom-complex is as follows: It represents an acute infectious disease of unknown origin and pathology, characterized by a short incubation period (four to five days), a period of continuous fever accompanied by intense headache, apathy, and prostration, and a profuse and extensive maculopapular eruption. The duration is about

two weeks, and the fever then ceases by lysis or crisis, after which all symptoms disappear. For years there was no evidence of mortality or contagion. A few examples of apparent contagion of Brill's disease are given in Friedman's monograph (1911) while Brill himself in the same year gives very full particulars of his one fatal case in which death occurred on the tenth day. In this instance the disease could not be communicated to animals.

In considering the possible identity of Brill's disease with typhus, we may note that the so-called "sporadic typhus" seen at times in localities in which epidemic typhus occurs, and which has always been mentioned by authors, does not apparently differ essentially from Brill's disease, and this is also partially true of the milder cases which occur in the midst of an epidemic, although such cases may well be as contagious as any others. Even entire epidemics of genuine typhus have sometimes, especially of late years, shown a low virulence and mild course. In order to appreciate the significance of a gradual decrease in the severity of these epidemics we must bear in mind that modern sanitation does not tolerate the overcrowding which once was a leading factor in the prevalence and deadliness of the disease.

The history of typhus in the United States is confined to a few epidemics, severe or mild, brought evidently from countries in which the disease is epidemic. The last of these was in 1892 and it was conceded that there had never been the least endemic persistence of any of these epidemics. In 1895 Hubbard saw at the Riverside Hospital in New York cases of a "pseudo-typhus," but nothing was subsequently heard of them. In 1896 Brill first began to note the affection which goes by his name in his hospital (Mt. Sinai) practice, and chiefly in Russian immigrants who of course came from regions not spared in past years by typhus, severe and mild. He kept track of such cases for fourteen years before making public the results of his observations; and by this time had controlled a material of 221. Had there been any specific bacterium or biological reaction known for typhus, as for typhoid, there would of course have been no problem of identity. As it was, but two resources were available —first inoculation experiments with animals, and second further clinical investigation of the two supposedly distinct maladies. The former have given conflicting results, although the positive finds of Anderson and Goldberger can hardly be explained away. In regard to the latter, we have cumulative evidence of the existence of the Brill syndrome in other countries and under other circumstances; and proofs also that it may exceptionally be both contagious and fatal. EDWARD PREBLE.

Brinton, Daniel Garrison.—Born in Chester County, Pa., May 13, 1837. He received the degree of Doctor of Medicine from Jefferson Medical College, Philadelphia, in 1860. He entered the United States Army in 1862 as Acting Assistant Surgeon, and in August, 1865, he was discharged with the rank of Brevet Lieutenant Colonel. In 1867 he became assistant editor of the *Philadelphia Medical and Surgical Reporter*, and subsequently its editor; also editor of the Half-yearly Compendium of Medical Science. Dr. Brinton was greatly interested in historical, antiquarian, and philosophical questions, and was in his time among the foremost ethnologists of America. He wrote many monographs and treatises on topics of this nature. A few of the more important of these may here be mentioned: "The Floridian Peninsula —its Literary History, Indian Tribes, and Antiquities," 1861; "The Shawnees and their Migrations," 1866; "The National Legend of the Chatha-Muskokee Tribes"; "The Myths of the New World," 1868; "The Phonetic Alphabet of Yucatan," 1870; and "The Religious Sentiment—a Contribution to the Science and Philosophy of Religion," 1876; "Aboriginal American Authors and their Productions," 1883; "The Iroquois Book of Rites," 1883; "Races and Peoples," 1890; "Religion of Primitive Peoples," 1897. He died at Atlantic City, N. J., July 31, 1899. A. H. B.

British Medical Association.—The British Medical Association was founded in 1832 at Worcester, Eng., by Dr., later Sir Charles Hastings, and has continued an uninterruptedly active course during the past eighty-one years. It was formed for the purpose of associating, for mutual benefit, the practitioners outside of London. The name adopted was the "Provincial Medical and Surgical Association." In 1856 it enlarged its scope and became the British Medical Association. It was incorporated in 1874 and reincorporated in 1909, with greatly increased powers and more freedom of action.

From its earliest inception, in addition to its professional and scientific work, it has kept in view the moral and hygienic welfare of the public. The history of the Association reflects the advance from the ignorance and crudeness of the early nineteenth century to the enlightenment of the present day. It has inaugurated and carried to a successful issue many of the reforms that have taken place, and its advice has been asked and its influence sought in nearly every undertaking of such a character. Public health laws, housing of the poor, reform of the poor-house and infirmary, baby-farming, care of the feeble-minded and insane, naval and army hygiene, and innumerable kindred reforms are in a great measure due to its efforts. On purely professional matters it has been equally active, and although it is frequently criticised by its members, it works constantly and earnestly for the betterment of medicine. It is the recognized representative body of the medical profession in Great Britain, and with a membership of over 23,000 and an annual income of over two hundred and fifty thousand dollars, it is enabled to exercise an important and powerful influence.

ORGANIZATION.—The *Division* is the unit of the Association. In its formation it is guided by geographical and numerical conditions. The object is to establish a membership of 500 who are within easy access of common centers for meeting. It manages its business as it thinks proper and meets as often as it considers desirable. Each Division elects delegates to the *Representative Body*, one for the first 200 members, another for the second 200, and an additional one for each succeeding 600. To facilitate work a number of divisions may unite to form a *Branch*.

The control of the Association is in the hands of the Representative Body, which meets prior to the annual meeting and at such other times as is necessary. Upon all important questions the views of the Divisions are obtained and the representative casts his vote accordingly. In addition to the elected members, the Navy and Army, and the Colonial Branches are represented.

The Representative Body appoints an Executive Council which is the business directorate and during the year carries out the details and oversees the work of the Association. At the annual Representative meeting certain standing committees are appointed which have control of matters relating to their particular subject and report annually. These are Ethical, Medicopolitical, Parliamentary Bills, Organization, Colonial, Hospitals, Naval and Military, Public Health, and Scientific Grants. In addition special committees are appointed from time to time such as those on Chloroform, Vaccination, Uterine Cancer, Modern Treatment of Fractures. As an instance of these special committees, on the request of

the "Fish Mongers Company" one was appointed to report upon the bacteria in shell-fish and what measures should be adopted to render shell fish suitable for consumption. All the reports are particularly valuable as they represent the latest word upon the subject, presented by practical and experienced workers. The chairman of the Representative meeting and the chairman of the Council hold the most important offices and upon their shoulders rest great responsibilities. The actual work of the Association is performed by the Financial or General Secretary, the Medical Secretary, the Editor, the Treasurer, and their staff of officials.

Membership.—All regular practitioners throughout the British Empire who are legally qualified to practise, are eligible for membership. They are elected by the Council after approval by the Division through which this application is made. The annual fee is twenty-five shillings, of which four are returned to the Division. This amount entitles the member to the *Journal* and all the privileges of the Association.

Meetings.—The meetings of the Association are held annually in the large cities. On two occasions they have taken place in Canada—at Montreal in 1897, and in 1906 at Toronto. The President is selected from the city in which the meeting is to take place, and he is usually informally nominated by the local Division. In 1847 the meeting for the first time divided into Sections, forming those on Medicine, Surgery, Midwifery and Physiology. These now vary, the usual number being about twenty or twenty-two—on Anesthesia, Anatomy, Bacteriology, Dermatology, Children's Diseases, Electrotherapeutics, Gynecology and Obstetrics, Laryngology and Rhinology, Medicine, Navy and Army, Neurology and Psychology, Ophthalmology, Otology, Pathology, Therapeutics, Physiology, State Medicine, Surgery, Tropical Medicine.

Building.—The offices of the Association are in its own building, situated at 429, Strand, London, W. C. This is an imposing structure, erected in 1909 and valued at some three-quarters of a million dollars. In it are also a valuable library, reading-room, writing room, and all the convenience of a club for those visiting London.

Journal.—The *Journal* was established in 1840 as the *Provincial Medical and Surgical Journal*. In 1844 it was taken over by the Association and in 1856 it changed its name with the Association and became the *British Medical Journal*. It is printed by the Association in its own printing offices.

Scientific Grants.—To encourage scientific research, annual grants have been made since 1874 These are now the Ernest Hart Memorial Scholarship, for research in State Medicine, of the value of one thousand dollars, tenable for one year, and renewable for three years; two Research Scholarships of the value of seven hundred and fifty dollars, for work in any branch of medical science. Also there are numerous grants of smaller amounts to the extent of two thousand dollars to research workers in various laboratories. The reports in 1912 were upon the following subjects: "Anemia of ankylostomiasis," "Flies and other insects as carriers of 'infection'" "Opsonic index in plague vaccination," "Destruction of alkaloids by emulsions of body tissues," "Study of experimental purpura," "Operative treatment of fractures," "Acute and subacute lesions of the spinal cord through infection of its lymph system," and "Cytology of the blood in passive immunity." Beaumont Small.

Broca, Paul.—Born in Sainte-Foy-la-Grande, France, June 28, 1824. At the earnest wish of his parents he chose medicine as his profession and began the study of this branch of knowledge at the University of Paris in 1841. He received the degree of Doctor of Medicine in 1849, and during the following ten years—by the character of the work which he did in the domain of pathological anatomy and in that of surgery, by his attractiveness as a lecturer, and by the conspicuous merit of his published writings—he attained a great and well-merited reputation in the medical world. In 1859, however, under the stimulus imparted by the works of Geoffroy-Saint-Hilaire, Serres, and Quatrefages, he began to devote himself with enthusiasm to anthropology. His numerous writings on topics belonging to this department of science will be found in the *Journal de physiologie*, and in the Bulletins and Mémoires of the Société d'Anthropologie. Among the most valuable of these, his essays on the functions of the brain, on brain-localization, and on aphasia (or aphemia) certainly deserve to be mentioned first. The third left frontal convolution of the cerebrum, in which he located the speech centers, is known still as Broca's convolution.

Fig. 1141.—Paul Broca.

Broca, however, did not confine his work within the more strictly scientific limits of the domains of neurology and anthropology; in the later period of his life he interested himself in the broad subject of public health, in the education of the people, in infant mortality, in the organization of a sanitary service in the French Army, etc. In recognition of the valuable services which he was thus rendering to the nation the Senate of France elected him a senator for life. His death occurred on July 8, 1880. (Pagel.) A. H. B.

Brodhurst, Bernard Edward.—Born in Newark, England, February 4, 1822. He studied medicine at the London Hospital and became an M. R. C. S. in 1844. In 1846 he went to the Continent to study and was in Rome in 1848 when the French troops under Gen. Oudinat advanced upon the city, then occupied by the Garibaldians. The unexpected resistance of the latter resulted in severe loss to the French. Three hundred of their wounded were taken to S. Spirito and other hospitals in Rome, but owing to the intense feeling against them they feared the Italian surgeons and begged to be placed under the care of foreigners. The Triumvirs therefore requested Brodhurst to minister to them which he did with such devotion that the French Government rewarded him with the Cross of the Legion of Honor. Returning to London, Brodhurst was appointed to the staff of the Royal Orthopædic Hospital where he served as surgeon to the time of his death. He was also surgeon to the Royal Hospital for Incurables and consulting surgeon to the Royal Hospital for Children. He was elected F. R. C. S. in 1859. In 1863 he was appointed assistant surgeon and in 1869 orthopedic surgeon to St. George's Hospital, where he was also lecturer on orthopedic surgery. He died, January 30, 1900.

Brodhurst made many contributions to the literature of orthopedic surgery, of which the following are the most important: "On the Nature and Treatment of Club-foot and Analogous Distortions Involving the Tibiotarsal Articulation," London, 1856; "Practical Observations on the Diseases of the Joints, Involving Anchylosis, and on the Treatment for the Restoration of Motion," 3d edition, London, 1861; "The Deformities of the Human Body—A System of Orthopedic Surgery," London, 1871; "On Anchylosis and the Treatment for the Removal of Deformity and the Restoration of Mobility in Various Joints," London, 1881; "On Curvature and Diseases of the Spine," London, 1883, and a second edition, 1888; "On the Nature and Treatment of Talipes Equinovarus, or Club-foot," London, 1893. T. L. S.

Brodie, Benjamin.—Born at Winterslow, Wiltshire, England, June 8, 1783. Having chosen medicine as his profession he went to London in 1801 and attended the lectures of John Abernethy. In 1808 he was appointed Assistant Surgeon to St. George's Hospital. In 1810 he was elected a fellow of the Royal Society. About this time he made numerous contributions, chiefly on physiological subjects, to periodical medical literature, and also published "Pathological and Surgical Observations on the Diseases of Joints," a work of considerable merit. In 1822 he received the appointment of Surgeon to St. George's Hospital. In 1828 he was made surgeon of the King, and in 1834 he was knighted. During this period of his career(1825–1845) Sir Benjamin Brodie ranked as the leading surgeon of London. Among his later publications the following deserve to be mentioned: "Lectures on Diseases of the Urinary Organs"; "Lectures Illustrative of Certain Nervous Affections"; "Clinical Lectures on Surgery"; and "Lectures Illustrative of Various Subjects in Pathology and Surgery." He died October 21, 1862. A. H. B.

Bromal Hydrate.—$CBr_3.COH + H_2O$. Like chloral, *bromal* is an oily fluid which, uniting with water, forms a crystalline hydrate. Bromal hydrate occurs in white crystalline masses of a sharp, burning odor and taste, fusible at 53.5° C. (128.3° F.), and soluble in water. Physiologically the drug is severely irritant, and, absorbed into the circulation, has been found by experiment (Steinauer) to cause restlessness followed by sleep, and, if the dosage be pushed, dyspnea, convulsions, and death. It may relieve pain, and has been thought to be of avail in averting threatened epileptic fits, but it is not official in the United States Pharmacopœia and is little used in medicine. It has been given in three-grain doses (Steinauer), but it is so disturbing to the digestive functions that the dose must be given in great dilution.

R. J. E. Scott.

Bromalin.—Hexamethylene-tetramine-bromethylate, bromethylformine $(CH_2)_6NHC_2H_5Br$, made by acting upon hexamethylene tetramine with ethyl bromide. It is in colorless scales or a white crystalline powder, almost tasteless and freely soluble in water. It is decomposed by heat. Bromalin was introduced to take the place of the alkaline bromides in epilepsy, and may be used in other conditions in which bromides are indicated. The dose is gr. xv.–lx. (1.0–4.0), and even large quantities are said not to cause bromism. W. A. Bastedo.

Bromamide.—Tribromaniline-hydrobromide, $C_6H_2Br_3.NH_2HBr$, is produced by reducing nitrotribenzol by nascent hydrogen and then acting upon this with hydrobromic acid. It occurs in colorless acicular crystals without odor or taste and is readily volatilized by heat. It is insoluble in cold alcohol, soluble in sixteen parts of boiling alcohol, and in chloroform, ether, and fixed oils. As an analgesic, sedative, and antipyretic it has been known to act promptly and effectively in acute and chronic rheumatism and neuralgia. Dose: gr. v.–xv. (0.3–1.0) in powder or capsule several times a day. W. A. Bastedo.

Bromeliaceæ.—A family of some forty genera and probably five hundred species, almost entirely tropical, in both hemispheres, a few subtropical. The family, by virtue of its structure, epiphytic habits and relations, is one of the most interesting known to botanists, and very many of its members are highly ornamental. Its economic importance is considerable. The pineapple is its most important product. The leaves of many species are important fiber-yielders, and the well-known "Florida moss" or "black moss" (*Tillandsia usneoides* L.) has many uses. The digesting power of pineapple juice upon albumin has been utilized in diphtheria to a slight extent. Its value as an aid to stomach digestion is probably of far greater importance, and the same property appears to exist in some of the leaf juices.

Henry H. Rusby.

Bromides.—General Medicinal Properties of the Bromides.—Compounds of bromine, whose basylous radicle is innocuous enough to permit of their medicinal administration in decided quantity, all show a certain influence over the animal system, commonly, and undoubtedly rightly, referred to the action of the bromine of their composition. Of the effects, the most striking feature is derangement of nerve function, which, in moderate dosage, takes the form of a deadening of reflex irritability, cerebral and spinal, and in poisonous administration shows itself as failure of power, voluntary as well as reflex, in the cerebrospinal centers. Clinically, the prominent effects are that the nervous, agitated, and wakeful subject becomes calm, tranquil, and predisposed to sleep; that convulsive seizures, the expressions of unnatural reflex irritability, such as the convulsions of epilepsy and of tetanus, tend to abate in frequency and violence; that a qualmish stomach becomes quieted, that tickling of the fauces fails to provoke gagging, and that sexual eagerness and even power wane. In profounder bromism what was at first intellectual laziness and indifference becomes positive stupidity, with failure of memory and with or without a certain grade of aphasia; what was a dulness of reflex activity passes to motor and sensory weakness—paresis of sight, hearing, and tactile sense and profound muscular debility, until at last, after apparently total abolition of all conscious existence, the poisoned subject dies, either from respiratory or from cardiac failure. Minor effects, in cases of continuous bromide medication, are a peculiar fetor to the breath, a tendency to an acneiform eruption, most pronounced on the face, arms, back, and buttocks, and a tendency to congestion and even edema of the fauces and uvula, and, later, of the conjunctiva also. All of these various symptoms, formidable though many of them are, rapidly abate upon discontinuance of the medicine, and, as a rule, have no permanent morbid results. Other effects, notably derangement of the circulation and lowering of body temperature, are observed in the operation of the most commonly used bromide, namely, the potassium salt, and also in that of the closely allied lithium bromide; but inasmuch as these are effects which are more or less common to all salts of potassium and lithium, it is an open question whether their occurrence in the present connection is not due rather to the basylous element of the bromide than to the bromine. Bromides are quick of

absorption, and, generally speaking, fairly quick of elimination, and in such elimination are to be found in all the secretions—urine, feces, sweat, saliva, and even in the pus of the acne pustules.

The most interesting effect of bromides, namely, the derangement of function of the cerebrospinal nervous system, has been made the theme of much experimentation for the purpose of finding just where the bromide influence strikes. As usual, the experiments are not wholly in accord, but their general drift clearly indicates, as H. C. Wood points out, that the deadening of functional activity occurs first and most severely in the peripheral ends of the afferent nerves and those portions of the axis that have to do with the reception of sensory impressions and their transmission as an impetus for motor reflex response. Later, and to a proportionately lesser degree, are affected the motor tract of the cord and the motor nerves. By this hypothesis is rendered intelligible the oft-observed occurrence that a bromized frog, while profoundly indifferent to pricks or searings, from evident cutaneous anesthesia, may still retain enough command of motor power to hop, and vigorously, too, at will.

The *therapeutics* of the bromides consist of the direct application, for clinical ends, of the bromine influence to blunt nervous impressibility. Such displays of nervous excitement as are the expression of a state of direct morbid irritation of the nervous system, in whole or in part, are conditions proper for the action of a bromide; but, on the other hand, the derangements of nerve function caused by *exhaustion*, general or local, are distinctly *not* to be treated by bromine medication. For in such latter case, because of the generally depressing character of the bromine influence, the exhaustion will be deepened, and the nervous symptoms, therefore, intensified. Prominent illustrations of the conditions in which bromides may be of benefit are undue restlessness and wakefulness, or mental irritability or morbidness from any emotional cause, or from severe intellectual labor under pressure; undue excitability of a lusty sexual apparatus from too free indulgence; and, more notable still, expressions of reflex action, such as the convulsions of epilepsy, of tetanus, or of strychnine poisoning; the convulsions of children, seasickness, or the vomiting of pregnancy or of neurotic poisoning. Conditions in which, on the other hand, bromides are useless or harmful are restlessness, wakefulness, or mental derangement from want of sleep, from starvation, from loss of blood, or devitalization from a prostrating disease, such as typhoid fever, or, locally, irritability of the sexual organs when associated with beginning of failure of power through exhaustion from excessive abuse. In cases for which bromides are fitting it is hardly necessary to say that the remedy will promise more if resorted to at the outset, and that large doses may conquer where small ones will utterly fail. In chronic and intractable disease, such as epilepsy, two points, besides sufficiency of dosage, must be observed, as follows: *First*, the blood must be kept evenly and continuously charged with the bromide salt. And, by reason of the rapid elimination of the salt, this result can be secured only by giving the daily allowance in at least three doses, whereof the evening one, having longer to last, should be larger than the others. *Secondly*, the medication must not be too speedily discontinued after apparent cure of the malady, but, on the contrary, must be kept up for months, and even years, thereafter. In epilepsy, it is singular that the form of the disease called *petit mal* should be, as it is, distinctly less amenable to bromide medication than the classical form in which the fits are outspoken. In epilepsy, when the disease is recent and of the latter variety, the curative power of the bromides surpasses that of any other drug; but, as a rule, the remedy will have to be pushed to the development of a certain grade of bromism before benefit appears.

The Bromides Used in Medicine.—The bromides official in the United States Pharmacopœia are, among bases of the heavy metals, *zinc* bromide, and among those of the alkali metals and metals of the earth, *potassium*, *sodium*, *lithium*, *ammonium*, *strontium*, and *calcium* bromides. *Diluted hydrobromic acid* and *monobromated camphor* also may be mentioned as being, logically, bromides, and furthermore as showing in their action upon the animal system the peculiar bromine influence in addition to their other effects. Lastly, an ethereal bromide, namely, *monobromethane* ("bromide of ethyl," "hydrobromic ether"), although not official, has been used in medicine as an anesthetic. In the present article will be discussed only the bromides of the metals of the alkalies and earths, in which alone the bromine influence is the dominant medicinal virtue. For zinc bromide, see *Zinc;* for diluted hydrobromic acid, see *Hydrobromic Acid;* for monobromated camphor, see *Camphor;* and for monobromethane, see *Ethyl Bromide.*

Potassium Bromide.—Potassium bromide, KBr, is official in the United States Pharmacopœia as *Potassii Bromidum*, Potassium Bromide. It occurs in "colorless or white, cubical crystals or a granular powder; odorless, and having a strongly saline taste. Permanent in the air. Soluble in about 1.5 parts of water, and in about 180 parts of alcohol at 25° C. (77° F.); in less than 1 part of boiling water, and in 16 parts of boiling alcohol; also soluble in glycerin. On heating the salt upon platinum foil, it decrepitates; near 700° C. (1290° F.) it fuses without decomposing, and at a bright-red heat it volatilizes, communicating a violet color to the flame. Its aqueous solution one in twenty is neutral, or has only a scarcely perceptible alkaline reaction upon litmus paper" (U. S. P.). In some commercial samples the alkalinity is said to be decided, sufficiently so to enable the salt to precipitate alkaloids from solutions of their salts. Potassium bromide should be kept in well-stoppered bottles.

Potassium bromide is the most generally active, the best known, and the most commonly prescribed bromide. It is capable of producing to the highest degree the peculiar bromine effects already detailed, and also has a marked influence over the circulatory organs, and, if pushed to poisoning, a power to lower body temperature. The circulatory derangement consists first in a slowing and weakening of the heart's contractions, passing even to stoppage of the organ in diastole; and, secondly, a probable—but probable only—narrowing of the lumen of the smaller blood-vessels, through vasomotor spasm. Partly because of the effect upon the heart, and partly also because of the presumed effect upon the blood-vessels, potassium bromide is commonly held to induce partial capillary anemia, especially of the nerve centers—spinal cord and brain. And because of this anemia, in turn, it has been imagined by some, and become quite a text-book tradition with many, that the action upon the vascular organs is the only direct one that potassium bromide exerts, all the nervous phenomena being sweepingly accounted for as mere secondary consequences of a diminished blood supply to the cerebrospinal axis. To refute this notion it seems only necessary to cite on the one hand the fact that other bromides than the potassic which have but little of the depressing effect of the latter salt upon circulation yet show the bromine influence over nerve function, and, on the other hand, to note that cerebrospinal anemia, occurring as it can easily be made to do experimentally by other methods and to any degree, is, when so determined, never followed by the peculiar phenomena of bromism.

As the drug is medicinally given, the clinical effects of potassium bromide are a salty taste in the mouth, with a little increase in the flow of the saliva, and perhaps also some diuresis, an abatement of all forms of nervousness, fidgets, or even spasms, with a tendency to mental calm and indifference, intellec-

tual and physical sloth, and, if circumstances favor, drowsiness. Along with these suggestive symptoms the pulse falls somewhat in force and frequency. If the dose has been single and not overlarge, little other than the foregoing effects will be declared; but, if the taking be continuous and the doses range high, the derangement may be profound, the subject presenting the picture of one mentally dull even to idiocy, with perhaps some aphasia; dull of hearing, sight, and feeling; physically weak even to paresis, sexually impotent, and with the peculiar symptoms of a fetid breath, a whispering voice, a face broken out in acne, a congested or even edematous faucial arch, a slow and failing pulse and respiration, and a depressed body temperature. In overwhelming dosage, paralysis of sense and motion becomes absolute, and death ensues quietly by failure of respiration or of cardiac action—the former if the poisoning has been progressive by accumulating small doses, the latter if by a single overpowering charge. But, as usual with the bromides, so long as the condition is one short of death, the symptoms quite certainly will ameliorate—and that, too, without lasting results—upon stopping the medication. In case of serious poisoning, the treatment must be in accordance with general principles, consisting in evacuation of the stomach, if a large single dose has been taken, and, for the rest, the employment of measures addressed to maintaining the action of the heart and lungs.

Potassium bromide is used, medicinally, exclusively for the peculiar purposes of the bromides generally, as set forth in the first section of this article. When the need is transient only, as to quiet a squeamish stomach, or to calm a restless subject and invite sleep, the dose will range from gr. xx. to xlv. (1.3 to 3.0), according to the intensity of the disturbance and the susceptibility of the individual. (The Pharmacopœia gives fifteen grains (one gram) as the average dose.) When, on the other hand, a continuous and powerful impression is necessary, as in treating epilepsy or tetanus, the doses may have to be both large and frequent. In dealing with epilepsy, the daily quantity will rarely be less than 90 grains (6.0) and may need to reach half an ounce (15.0), given broken up into three or four doses evenly distributed over the waking hours, excepting as to the evening portion, which should be somewhat larger than the others. The actual dosage in a given case must be determined by the effects produced. Even with the smallest daily quantity above named a certain degree of "bromism" will follow the continuous giving, and such result must be expected In tetanus or strychnine poisoning the dosage of bromide reaches its maximum. Here the extraordinarily he ghtened reflex irritability which is the essence of the morbid condition in the two affections makes the subject comparatively insusceptible to the benumbing influence of bromine. Even so large a dose as half an ounce (15.0) has been given at a single draught, and the daily total should certainly reach this figure. Yet in strychnine poisoning it must be remembered that the tetanus, if it does not kill within a couple of hours, then rapidly abates, and simultaneously, of course, disappears the insusceptibility to bromide influence. Care must be taken, therefore, to diminish the bromide dosing, as the morbid irritability fades, else, as has actually happened, the subject may be saved from death by strychnine convulsions only to be brought to the verge of the grave by bromide palsy. Potassium bromide is administered in solution either in simple iced water or what is pleasanter and in case of large doses makes the draught less obnoxious to the stomach, in water slightly alkalinized by the addition of a little sodium bicarbonate, or, best of all, in water both alkaline and effervescent, such as Vichy or Apollinaris.

Sodium Bromide.—The salt, NaBr, is official in the United States Pharmacopœia as *Sodii Bromidum*, Sodium Bromide. It occurs in "colorless or white, cubical crystals, or a white, granular powder, odorless, and having a saline, slightly bitter taste. The salt absorbs moisture from the air without deliquescing. Soluble in about 1.7 parts of water and in 12.5 parts of alcohol at 25° C. (77° F.); in 0.8 part of boiling water and in 11 parts of boiling alcohol. When heated to a bright red heat the salt melts, and, at a somewhat higher temperature, slowly volatilizes without decomposition. To a non-luminous flame it imparts an intense, yellow color. An aqueous solution (one in twenty) is neutral, or shows a faintly alkaline reaction with red litmus paper" (U. S. P.). Sodium bromide is hygroscopic, and should be kept in well-stoppered bottles.

Sodium bromide is less unpleasant to taste than the potassium salt, and is in every way less deranging of function. But yet, despite the fact that its innocuousness permits of its prescription in larger doses and for more continuous administration than may be possible with potassium bromide, the bulk of testimony goes to show that the sodium salt is of distinctly inferior curative power. Its use is, therefore, properly confined either to cases in which but a mild effect is called for, or to those in which, for any reason, the potassium salt cannot be given, or having been given must be abandoned. The fact that, weight for weight, the sodium bromide contains more bromine than the potassium (in the proportion of 77.62 to 67.13) simply shows the more forcibly the intrinsic physiological feebleness of the compound. Sodium bromide should be given in the same manner as the potassium salt, and in the same dose, carefully to be augmented according to the effects produced.

Lithium Bromide.—The salt, LiBr, is official in the United States Pharmacopœia as *Lithii Bromidum*, Lithium Bromide. It occurs as a "white, granular salt, odorless, and having a sharp, slightly bitter taste; very deliquescent. Soluble in 0.6 part of water at 25° C. (77° F.), and in 0.3 part of boiling water; very soluble in alcohol; also soluble in ether. At a low red heat the salt fuses, and at a higher heat it is slowly volatilized. It imparts a crimson color to a non-luminous flame. The aqueous solution is neutral to litmus paper" (U. S. P.). Being exceedingly deliquescent, this salt should be kept in well-stoppered bottles.

So far as observed, lithium bromide very closely resembles the potassium salt in its effects, as the nature of its base would render likely; but it is more speedily and more powerfully hypnotic than the potassium salt. It has the demerit of comparative costliness. It contains proportionally more bromine than does any other of the alkaline bromides (containing ninety-two per cent.), and has been recommended in one-half the dose of the potassium salt (Weir Mitchell); though the Pharmacopœia gives the average dose the same for both salts.

Ammonium Bromide.—The salt, NH_4Br, is official in the United States Pharmacopœia as *Ammonii Bromidum*, Ammonium Bromide. It occurs as "colorless, transparent, prismatic crystals, or a white, crystalline powder, odorless, of a pungent, saline taste, and permanent in dry air. Soluble in 1.2 parts of water and in 12.5 parts of alcohol at 25° C. (77° F.), in 0.7 part of boiling water and in nine parts of boiling alcohol. When heated, ammonium bromide volatilizes completely without fusing. An aqueous solution of the salt slightly reddens blue litmus paper" (U. S. P.).

From the point of view of the clinician, ammonium bromide may be regarded as substantially a duplicate of potassium bromide in medicinal virtues, while at the same time more acrid in taste and in local action. It has been used for the same purposes as the potassium salt, and in the same dose, and has been strongly recommended by Brown-Séquard and others in

epilepsy. It is less depressing than potassium bromide.

Strontium Bromide.—The salt, $SrBr_2$, $6H_2O$, is official in the United States Pharmacopœia as *Strontii Bromidum*, Strontium Bromide. It is in "colorless, transparent, hexagonal crystals; odorless, and having a bitter, saline taste. Very deliquescent. Soluble in about one part of water at 25° C. (77° F.) and in 0.4 part of boiling water. It is readily soluble in alcohol, and is precipitated from this solution upon the addition of an equal volume of ether, in which it is insoluble. When heated the crystals at first melt and then lose all their water (30.4 per cent.). The anhydrous salt fuses at 630° C. (1166° F.). To a non-luminous flame the salt communicates an intense, red color. Its aqueous solution is neutral to litmus paper" (U. S. P.). Owing to the extreme deliquescence of this salt it should be kept in glass-stoppered bottles.

As in the case of the strontium salts generally, this one closely resembles the potassium salt in its effects on the animal system. Compared with potassium bromide, however, strontium bromide is the better borne, having less tendency to derange digestion or to bring on the special symptoms of bromism. It may be prescribed in the same doses and for the same purposes as the bromides generally.

Calcium Bromide.—The salt, $CaBr_2$, is official in the United States Pharmacopœia as *Calcii Bromidum*, Calcium Bromide. It is a "white, granular salt, odorless, of a sharp, saline taste, and very deliquescent. Soluble in 0.5 part of water and in one part of alcohol at 25° C. (77° F.); more soluble at boiling temperatures. An aqueous solution of the salt is neutral to litmus paper" (U. S. P.). The salt must be kept in well-stoppered bottles.

Calcium bromide does not seem to differ materially in properties from potassium bromide, and stands in medicine as an additional and not over-necessary substitute for the same, in the same range of application and in the same dosage. EDWARD CURTIS.
R. J. E. SCOTT.

Bromidrosis.— Bromidrosis, or osmidrosis, as a disease *per se*, is a pathological variation in the odor-producing constituents of the sweat *as secreted*, is associated as a rule with the functional disorder of the sweat apparatus, hyperidrosis, and, like it, may be either local or general. This condition as such, if it occurs at all, is rare.

The condition ordinarily denominated bromidrosis is due, as was taught by Hebra to be the case in the majority of instances, to a rapid decomposition of the sweat *after* its secretion, with the resultant odor, warranting the term stinking applied to it.

When local, as is more commonly the case, the regions affected are those in which sweating oftenest occurs in excess and in which its quick evaporation is more or less retarded or prevented by the nature of the parts or their covering, as the axillæ, groins, anogenital region, and the feet—the last being by far the most frequent situation of the affection. Here the odor is marked and most characteristic, differing from the odor of other parts affected by its unmistakable, nauseating heaviness when once recognized—and one whiff is all-sufficient—the foul emanation rendering the near neighborhood of the unfortunate victim anything but pleasant, and sometimes impossible.

The change that takes place in the sweat is claimed to be due to the presence of a special microorganism—*Bacterium fœtidum*, a micrococcus which Thin of Prague recognized in sweat obtained from the feet. It has been shown by Parkes that soldiers with uncovered feet do not suffer from this affection, and he claims that the only cause of the disease, if such it can be called, is the covering of the feet, the absence of all coverings giving no opportunity for the development in the secretions of the special bacterium.

Treatment in general is linked with that of hyperidrosis. A level teaspoonful of the precipitated sulphur in milk twice daily has been highly recommended. It is an empirical remedy, the action of it not being explained by Crocker, who claims to have succeeded more often by this than by any other procedure, local treatment not being necessary with it. However, dusting finely powdered boric acid well in between the toes and rubbing it into the stockings and shoes daily will be found as efficient, cleanly, and convenient a local method as any yet devised, and some local treatment will generally have to be resorted to. Hot water applied as hot as can be borne for a few minutes before using the boric acid is a great aid.

If the sulphur treatment purges too freely, its action may be controlled by astringents. In five to ten grain doses salicylate of sodium may be found useful. This may be tried when patients object to the sulphur. It has cured some cases. Among other local remedies may be mentioned chromic acid; painted on the feet in five- to ten-per-cent. solution, according to the obstinacy of the case, every three to six weeks, it has been used successfully. Mutton suet with two-per-cent. salicylic acid is in general use in the German army for rubbing on the feet, and further has the advantage of a lubricant when much walking is to be done. Formalin in one- to ten-per-cent. strengths in alcohol is of value. It should be followed by the use of dusting powders. A one-per-cent. solution of permanganate of potassium has been well recommended. Various other remedies are extolled, but the boric acid will be found the best of all if preceded by the hot-water applications.

CHARLES TOWNSHEND DADE.

Bromine.—Bromine is official in the United States Pharmacopœia as *Bromum*, Bromine. It is described as "a heavy dark, brownish-red, mobile liquid, evolving, even at ordinary temperatures, reddish fumes, highly irritating to the eyes and lungs, and having a peculiar suffocating odor, resembling that of chlorine. Specific gravity, 2.990 at 15° C. (59° F). Boiling-point 63° C. (145.4° F.). Soluble in twenty-eight parts of water at 25° C. (77° F.), and readily soluble in alcohol or ether (with gradual decomposition of these liquids); also in carbon disulphide, and in chloroform, with a deep reddish-yellow color. On exposure to air or to heat it is completely volatilized without leaving any residue" (U. S. P.). Bromine has the same intense affinity for hydrogen that has chlorine, and so, in similar manner to chlorine, determines the oxidation of organic matter in the presence of moisture by appropriating the hydrogen of the water and liberating the oxygen. The fumes of bromine are thus deodorant, like chlorine. Mixed directly with foul-smelling or infectious matter, bromine is powerfully deodorant and disinfectant. Yet practically it is of little use in such capacity, by reason of its costliness, its bad smell, its caustic and bleaching tendency, and the exceedingly irritant action of its vapor upon the human air passages. Squibb estimates that an ounce of bromine, accidentally spilled in an ordinary chamber, would render the air thereof dangerous to life.

Locally applied to living animal tissues, pure bromine is a very searching and painful caustic, and non-caustic dilutions act as detergent and stimulant lotions to foul or sloughing ulcers. Here again, however, the cost of the remedy and its offensiveness render it less practicable than its efficiency would suggest. For caustic purposes, bromine is applied clear, the patient being etherized, if the area to be cauterized is at all extensive, and the operator taking

care that his eyes and nose do not come too near the fumes of the very volatile and pungent liquid. For a strong lotion, a ten-per-cent. solution in water may be employed, wherein the bromine is made to dissolve by the addition of one-third of its weight of potassium bromide. For weaker lotions—any percentage less than three—bromine is directly soluble in water without any saline addition. Taken internally, bromine is doubtless absorbed as a bromide. It was formerly used as an internal medicine in the class of diseases for which iodine or the alkaline iodides are now so extensively employed. For the specific purposes of the alkaline bromides (see *Bromides*), bromine is practically unavailable, because of its irritant action and offensive taste. Bromine has been given internally in the dose of from three to six drops of a two-and-a-half-per-cent. aqueous solution.

Toxicology.—Bromine is an intensely irritant, corrosive poison. The fumes, inhaled, produce extreme irritation of the eyes, the air passages, and even the stomach. Severe bronchitis, pulmonary hemorrhage and inflammation, and death may result. Swallowed in overdose, bromine produces the usual symptoms of the corrosive poisons, viz., intense gastric irritation, collapse, and death. An ounce of undiluted bromine, swallowed, produced death in seven and a half hours. In case of poisoning by inhalation, the local irritation should be treated by the breathing of the atomized spray of an alkaline solution, such as Dobell's solution. In poisoning by swallowing, the stomach must be washed out and ammonia given, largely diluted and mixed with olive oil.

Edward Curtis.
R. J. E. Scott.

Bromine-Arsenic Springs.—Ashe County, North Carolina.

Post-office.—Crumpler. Hotel.

Access.—Via Norfolk and Western Railroad to Marion, Virginia, for Trout Dale, Virginia, twenty miles from the Springs; or via the Southern Railway to Wilkesboro, North Carolina, forty miles from the Springs. Good mountain hacks are to be had for the trip.

This spring was discovered in 1885. Since that time it has come into extensive use, and its waters are widely sold. The location of the spring is in a mountainous district, midway between the Alleghany and the Blue Ridge Mountains, 3,000 feet above the sea level. The spring flows about sixty gallons hourly. The following analysis was made by Prof. Henry Froehling:

One United States Gallon Contains:

Solids.	Grains.
Sodium carbonate....	1.04
Calcium carbonate....	.93
Magnesium carbonate.	.62
Lithium carbonate....	.03
Copper carbonate.....	Trace.
Zinc carbonate.....	Trace.
Calcium fluoride.....	Trace.
Potassium sulphate..	.62
Potassium chloride....	.21
Sodium chloride.....	.65
Sodium arsenate	Trace.
Sodium iodide.....	Trace.
Sodium bromide.....	.04
Sodium borate.....	Trace.
Aluminum phosphate..	.12
Iron sulphate.....	.08
Silica.....	1.08
Organic matter.....	.03
Total.	5.45

The water is unique in possessing recognizable quantities of copper and zinc. It also contains the somewhat rare ingredients of arsenate of sodium and the iodide and bromide of sodium. We also find an appreciable amount of carbonate of lithium and sulphate of iron. The water is not highly mineralized, but it possesses valuable qualities as a mild antacid, tonic, and alterative. It is useful in many of the affections benefited by this class of waters.

Emma E. Walker.

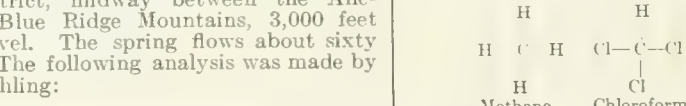
Bromine Chloride.—By direct union of the two elements, bromine and chlorine, a compound is formed appearing as a reddish-yellow, volatile, mobile fluid, soluble in water. This compound is powerfully caustic, but has never been used in regular medicine except as an ingredient of a caustic paste used by Landolfi, of Naples, for the treatment of cancer.

R. J. E. Scott.

Bromipin.—This is an addition product of oil of sesame, containing ten per cent. of bromine. It is a yellow fluid having the appearance of a fixed oil, and it has a bland, oleaginous taste. In spite of the large amount of bromine which it contains, the oil is non-irritating and may be given pure by mouth. It is readily absorbed and its action is of the same character as that of the alkaline bromides. Losio claims that it surpasses potassium bromide in chorea, epilepsy, and trigeminal neuralgia. Dornblüth found that one dram given at the evening meal would ward off a night attack of cardiac palpitation or angina pectoris. The oily taste of bromipin is not pleasant, but very soon the taste is acquired, and the patients continue to take it for a long time without gastric or intestinal disturbance. The dose is ℥ss.–ii. (2.0–8.0) daily for restlessness and nervous irritability; for chorea or epilepsy, up to ℥ss. (16.0) a day. It may be administered pure and unmixed, or with beer, or mixed with cacao, sugar, white of egg, and oil of cinnamon. A not unpleasant emulsion is made by taking two ounces of bromipin and emulsifying it with half an ounce of powdered acacia, half an ounce of syrup, and cinnamon or peppermint water to make four ounces, to be given in doses of from one to four drams (4.0–16.0).

W. A. Bastedo.

Bromoform.—Bromoform, $CHBr_3$, is analogous in its constitution to chloroform and iodoform.



It is official in the United States Pharmacopœia under the heading *Bromoformum*, bromoform. It is a liquid consisting of ninety-nine per cent. of bromoform and one per cent. of absolute alcohol. It is "a heavy, transparent, colorless, mobile liquid, with an ethereal odor, and a penetrating sweet taste resembling that of chloroform. Specific gravity: 2.808 at 25° C. (77° F.). Very slightly soluble in water, but soluble in all proportions in alcohol, ether, benzene, petroleum, benzin, and in the fixed and volatile oils." (U. S. P.)

It is formed by the action of acetone on sodium hypobromite. Bromoform has anesthetic properties, but not so marked as chloroform. It is a sedative, and has been used mainly in the treatment of whooping cough. There can be no doubt of its value in this disease; but attention should be directed to its toxic properties, several cases of poisoning having been reported, some of them proving fatal. The toxic effects are due to two causes: (1) The comparative difficulty of dispensing bromoform in a mixture, with the result that the last doses in the bottle con-

tain more bromoform than the earlier doses. (2) The decomposition of the bromoform, with liberation of bromine. The pharmacopœial dose is three minims (0.2). The drug may be dispensed in an emulsion, or dissolved in almond oil and given in capsules.

R. J. E. Scott.

Bromol.—Tribromphenol, $C_6H_2Br_3.OH.$, is obtained by the action of bromine on a solution of phenol. It is a crystalline substance, almost insoluble in water; soluble in alcohol, ether, glycerin, chloroform, and oils. Bromol is used as an antiseptic dressing for wounds, etc., in powder or ointment of four to ten per cent. strength, and is also administered as an intestinal antiseptic.

Its action is slow, and its use has been mainly limited to typhoid fever and cholera infantum. It is not dissolved by the gastric juice. The dose is gr. ss.–ij (0.03–0.13), and it is best given in a pill.

R. J. E. Scott.

Bromum.—See *Bromine*.

Bronchi, Anatomy of the.—As a preface to the histology of the bronchi, a short résumé of the gross anatomy seems here desirable. The term bronchi is the Latin equivalent of the Greek *βρόγχια*, the main bronchial tubes, derived from *βρόγχος*, trachea.

The bronchia, beginning at the tracheal bifurcation opposite the third dorsal vertebra (fourth in the female), terminate in the pulmonary lobules. The primary tracheal branches, from their distribution, are named the right and left bronchus. The former is shorter, larger, and more horizontal than the latter, and the septum bronchiale separating them is placed to the left of the longitudinal (in the recumbent posture of the body) axis of the treachea. Hence bodies falling into the trachea lodge more frequently in the right bronchus. Hyrtl teaches that postmortem examinations of the new-born, dying after a few respirations, show that the right lung respires before the left, and he explains the fact by the difference in size and location of the beginning of the right bronchus. The general rule of dichotomous subdivision obtains, but is not without exception; *e.g.* the right bronchus subdivides into three branches, one for each lobe. Occasional small branches are given off by the main trunk. Having reached the diameter of 0.21 millimeter ($\frac{1}{120}$ inch), they enter the apices of the pulmonary lobules. Here again branching at acute angles they dilate slightly, becoming funnel-shaped, whence the name "infundibula." (See article *Lungs, Anatomy of the.*)

Structure.—The bronchia are hollow, cylindrical tubes, which retain in structure, throughout a large portion of their extent, the characteristics of the trachea. Like the latter, they consist of four distinct layers: an external fibrous, a muscular, an internal elastic, and a mucous layer. Some authorities make five layers, dividing the external fibrous into two, viz., the adventitia, or loose connective tissue, and a fibro-cartilaginous layer within, which constitutes the actual skeleton of the bronchi. For convenience these two layers may be regarded as one.

The *External Fibrous Layer* consists of a dense meshwork of connective tissue, in which are to be found rings or laminæ of hyaline cartilage. In the primary bronchia these are disposed as in the trachea, *i.e.* in broken rings like the letter C, held together by fibrous bands. The ring is made complete by small transverse bundles of unstriped muscular fibers attached by microscopic tendons to the ends of the rings. By their contraction they increase the curvature of the cartilage and so diminish the caliber of the tube. The right bronchus contains six to eight of these cartilages; the left ten to twelve. Further removed from the trachea the cartilages gradually lose their ring-like shape, and are disposed in irregular polygonal laminæ. Becoming smaller and less frequent, they finally disappear in tubes of less diameter than 0.23 millimeter ($\frac{1}{110}$ inch), the fibrous layer still continuing to form the external coat.

The *Muscular Layer* lies within the fibrous layer just described. It consists of separate bundles of unstriped muscular fibers, disposed for the most part transversely to the tube; they are known to some as the muscles of Reisseissen. It is better developed in the intervals between the cartilages than just beneath them. As the cartilages disappear this muscular layer becomes better and better developed, until at last it completely surrounds the bronchioles, which, on

Fig. 1142. Represents a Transverse Section of the Bronchial Wall at the Fifth Bifurcation in the Human Adult. *a*, Epithelial layer of the mucous membrane; *b*, hyaline basement membrane, formed from *c*, internal elastic layer, showing its varying thickness; *d*, *d*, muscular layer; *e*, muciparous crypts; *f*, cartilaginous lamina; *g*, external layer; *h*, branch of bronchial artery. (× about 30 diameters.) (Drawn with camera by Dr. F. Cary.)

section, but for the epithelial lining, might be mistaken for arterioles. The muscular layer can be traced to the final branching of the bronchiole to form the alveolar passages, where, according to Rindfleisch, it becomes again better developed into a sort of "sphincter" at the point of entrance to the alveolar passages. The function of the muscular layer is to narrow the caliber of the tubes. This is manifested to any appreciable extent only in the bronchioles. The cartilages prevent any decided narrowing where they exist. In the experiments of Dr. C. J. B. Williams with electrical stimulation on bronchioles of less than a line in diameter, they were seen to contract until they nearly obliterated their lumen. Dr. Gairdner suggested that the contractility of the minute bronchioles may serve to expel collections of mucus which have accumulated in them, and which neither ciliary action nor the ordinary expiratory efforts would dislodge.

The Internal Elastic Layer.—Within the muscular layer, and beneath the mucous membrane, lie longitudinal bundles of elastic tissue quite regularly disposed. They project, as it were, partly into the lumen of the tube, and so give, on transverse section, a wavy, corrugated appearance to the lining membrane; on longitudinal section, a grooved or furrowed one. Piercing this as well as the muscular layer, chiefly in the bronchial tubes containing cartilages, are to be seen the muciparous ducts, lined with epithelium, leading inward to open on the free surface of the mucous membrane. The mucous crypts

lie in the external fibrous layer, chiefly in the intervals between the cartilages.

The *Mucous Membrane* of the bronchia and bronchioles, forming the internal layer, possesses, throughout the greater portion of its extent, the characteristics of that of the tracheal mucous membrane. Like the latter, it consists of epithelial cells of the ciliated columnar variety, superimposed upon a basement membrane, which latter is made by a condensation of the inner part of the internal elastic layer. When the tube has reached the diameter of 0.2 millimeter ($\frac{1}{50}$ inch), these cells lose their cilia, become shorter, smaller, and rounded, in the ultimate tubules becoming the simple pavement cells. Here the membrane loses its character as a mucous membrane,

FIG. 1143. *a*, A minute bronchiole splitting into the *ultimate* branches, which terminate in the alveolar passages; the epithelium has become of the simple pavement variety; on the left branch can be seen one of the so-called "saccular dilatations"; *b*, artery; *c*, medium-sized bronchiole having no cartilaginous lamina. The remainder of the field is normal lung tissue. (× about 30 diameters.) (Drawn by Dr. F. Cary, from a microscopical section, with camera.)

and resembles that which lines the alveoli (see article *Lungs, Anatomy of the.*) Here and there in the larger tubes are to be found the cup-shaped cells (*Becherzellen*) of Schulze. The mucous crypts are not only extremely numerous but relatively large. They are much more in evidence in the intercartilaginous intervals. As a rule they are small, racemose glands, often having a veritable excretory duct with ramifications. It is asserted that under normal conditions these glands are closed and furnish no secretions, but are very susceptible to the action of irritants of various kinds.

Vascular Supply.—From the thoracic aorta are given off the bronchial arteries, which, receiving occasionally branches from the first intercostal and internal mammary arteries, accompany closely the subdivisions of the bronchia, supplying their walls, the walls of the large pulmonary vessels, the lymphatic glands, and the connective tissue of the lungs, to terminate finally in capillaries which inosculate freely with the respiratory plexus. Injections thrown into these vessels will fill also the capillary plexus of the arteria pulmonalis. The corresponding bronchial veins empty in part into the vena azygos, in part into the vena pulmonalis; the venous radicles from the ultimate bronchioles emptying into the latter, those corresponding to the arterial branches to the bronchia and lymphatics, into the former.

Lymphatic Supply.—The lymphatics arise in the alveolar septa. Stomata open on the alveolar walls between the epithelial cells, communicating thus directly with the alveolar cavity. They form a plexus in the submucous tissues, accompany the branches of the bronchia, as well as the pulmonary veins and arteries, emptying finally into the bronchial glands at the roots of the lungs. Within the lungs they often possess a gray or black speckled appearance, from the absorption of pigment or foreign bodies.

Nerve Supply.—The nerve supply to the lungs is derived from the pulmonary plexuses formed from branches of the vagus and sympatheticus. The filaments from these plexuses—situated at the lung hilum—follow the ramifications of the bronchia, becoming lost finally on them, and in the parenchyma of the lungs. When carefully stained they are seen to possess, in parts of their course, the microscopic ganglia to which Remak and Schiff first called attention.

The sensibility of the bronchia must be very slight; at least this seems to be true of their smaller branches, because of the slight complaint made by consumptives in whom large portions of bronchial and lung structure are being destroyed. LEWIS L. MCARTHUR.

Bronchial Glands, Diseases of the.—The bronchial glands are subject to the following pathic processes:

1. Inflammations: (*a*) acute; (*b*) chronic.
2. Morbid deposits and growths: (*a*) pigmentation; (*b*) cancer; (*c*) tubercle; (*d*) tertiary syphilitic growths; (*e*) albuminoid disease.

ANATOMY.—Since the greater number of the symptoms arising from disease in the bronchial glands are due to implication of adjacent parts, either through inflammation or from pressure, exact knowledge of the anatomical relations is of the utmost value in determining the significance of any given symptom.

The largest group of glands lies just below the bifurcation of the trachea, between the right and the left bronchus. They are in relation, laterally, with the bronchi; anteriorly, with the pericardium, arch of the aorta, and pulmonary artery; and posteriorly with the aorta, vena azygos, esophagus, and pulmonary plexus of nerves. Smaller ganglia are situated upon the anterior, posterior, and superior surfaces of the right and left bronchi. Those upon the right are the larger, and are in relation with the arch of the aorta, the brachiocephalic and subclavian arteries, the brachiocephalic and azygos veins, and the pneumogastric and recurrent laryngeal nerves. On the left they are in relation with the extremity of the arch of the aorta, the origin of the left subclavian and common carotid arteries, the subclavian vein, and the pneumogastric nerve with its recurrent branch.

Afferent vessels reach the glands from the lungs, pleuræ, neck, etc. The blood supply is through the bronchial arteries.

PATHOLOGY AND MORBID ANATOMY.—The pathic processes which occur in the bronchial glands are in no respect different from those which take place in other lympathic glands. The resulting anatomical changes assume special importance through their mechanical effects.

1. *Acute inflammation* is attended by cellular infiltration, with increase of lymphoid elements and retention of lymph, resulting in enlargement of the glands and softening of their parenchyma. When this process is rapid, or if due to specific poisons, suppurative and necrotic changes may follow. More commonly resolution takes place, and the glands return to their normal size.

2. *Chronic inflammation* is characterized by similar but more gradual cellular and lymphoid changes. In connection with these, fibrous growth is more marked; the glands become greatly enlarged, in some cases permanently, and their capsules are thickened and form adhesions with surrounding tissues. Resolution

is seldom complete, and if it is long delayed the glands become contracted and indurated.

When suppuration results, the pus may find its way by an ulcerative process to the free surface of a bronchus, into the esophagus or pericardium, or into the substance of the lung or lumen of a blood-vessel; or the contents of the abscess may undergo caseous, calcareous, or cystic degeneration. Even in the acute form suppuration rarely takes place with sufficient rapidity to allow rupture directly into the connective tissue, and in the chronic forms protective inflammation with adhesion is always present.

3. *The specific inflammatory changes* present no peculiarities in pathological processes.

4. *Pigmentation.*—Carbonaceous and other deposits in the bronchial glands seldom cause more than the lightest grades of inflammatory changes. The glands become more or less enlarged and variously pigmented. In extreme cases they are entirely black, firm, hard, and gritty on section, resembling a lump of coal. The glandular tissue is partially atrophied and absorbed. When suppurative changes supervene, the discharge from the resulting abscess is at first black, and, though gradually becoming lighter, is not entirely free from pigment until the entire gland has been removed.

5. *Cancer.*—Cancerous developments in the bronchial glands follow similar disease of the lungs, pleura, or mediastinum, and are of like character. Primary cancer is infrequent.

6. *Tubercle.*—Secondary tuberculosis occurs, to a greater or less degree, in all cases of pulmonary phthisis. In children, the glandular changes are often the more extensive and important, or may even represent a primary infection. The process is commonly one of general infiltration, evenly distributed throughout the gland. It is seldom that the deposit presents the form of gray miliary tubercle. In connection with these changes the glands enlarge, and at first are softer than normal, but, as the process advances and implicates the entire gland, they become firm and resistant, resembling tuberculous pulmonary consolidation. In the second stage the usual softening takes place, and tuberculous glandular abscesses are formed which follow the course of other abscesses described above.

7. *Syphilis.*—Syphilitic deposits are usually tertiary. Gummy deposits may lead to extensive enlargement, with subsequent caseous or suppurative degeneration.

8. *Albuminoid degeneration* is exceedingly rare. When present, the glands are usually enlarged, firm, and tense; occasionally they are atrophied. On section they present the usual waxy, glistening, homogeneous appearance, and give the characteristic reaction with iodine.

Etiology.—The lymphatic diathesis and general malnutrition are here, as elsewhere in the body, predisposing causes of glandular disease. Some statistics have seemed to show a slightly greater predisposition among females, and an increasing liability to such disease after puberty.

West and others consider the disease to be very frequent among infants and young children.

Of the exciting causes, acute inflammation of the pulmonary tissue or pleura is the most frequent. Thus, a simple bronchitis, a pneumonia, a pleurisy, or an empyema, etc., may each be followed by an acute or chronic inflammation of the bronchial glands, resulting in resolution, abscess, or caseous degeneration.

So frequently have these glands been found enlarged in cases of whooping-cough that Noël Guéneau de Mussy was led to regard the spasmodic element in the cough as due to pressure upon the pneumogastrics by the enlarged glands. Others, however, have reported cases in which the pneumogastrics were not only pressed upon, but even involved in the inflammatory processes surrounding the gland, without the presence of any cough.

Both acute and chronic inflammatory changes have been observed in the bronchial glands in connection with most of the infectious diseases, more especially in typhoid fever, measles, scarlet fever, and pyemia. In these conditions the changes are part of a general lymphatic inflammation, and are seldom of sufficient extent to attract attention during the life of the patient.

Absorption of various forms of dust to which certain classes of workmen are exposed, with the consequent filling and clogging of the glandular passages, may lead to either acute or chronic inflammation, ending in atrophy or suppuration and abscess. Such a result is exceedingly rare, however, if we consider the number of cases of pneumonoconiosis in which the glands become partially or completely filled with extraneous matter.

As already indicated in the sections on classification and pathology, the specific causes of cancer, tubercle, syphilis, and amyloid degeneration are exciting causes of disease in these glands.

Finally, many cases of enlargement, induration, or suppuration with secondary changes will be found in which no exciting cause is apparent beyond the lymphatic diathesis. Simple inflammation seldom causes suppuration, such a result following more certainly from septic irritation or tubercle.

Symptoms.—In the earlier stages, and, indeed, throughout the entire course of the disease, unless the glands form decided tumors, the symptoms will be almost entirely rational. Since they are due solely to pressure, and as the glands involved in different cases will not be the same, nor always enlarge in the same direction, it is evident that the symptoms will vary greatly in their order of development and relative importance in different cases.

In many instances, even when the glandular disease is slight, the anatomical disturbances may cause such marked symptoms as to obscure, or divert attention from, the more serious precedent conditions.

1. *Cough* is the most frequent as well as the earliest symptom. This may be due to pressure upon either a bronchial tube or the recurrent laryngeal nerve. In the former case it will resemble the cough of simple bronchitis. When due to pressure on the nerve it will be more harsh and laryngeal in character, and in some cases will have a distinct spasmodic element. When the irritation is severe it may be a persistent dry hacking, with or without paroxysmal exacerbations. More rarely it is deep, hollow, and metallic, or resembles the cough of an animal.

2. *Expectoration* attending the bronchial form of cough is quite constant. At first white and frothy, it gradually becomes mucopurulent when the glandular processes are acute and rapidly extending, or changes to a tenacious, mucous sputum with the more chronic processes. Should a glandular abscess open into the bronchial tubes, it will be evidenced by a more or less free purulent expectoration, mingled, it may be, with cheesy or even calcareous matter. After such an opening has occurred, an intermittent purulent discharge will continue indefinitely, or until the abscess has healed. When cough is due to nerve compression, expectoration is slight or entirely absent. No appreciable modification in the expectoration will be observed when the glandular disease is secondary to other pulmonary lesions.

3. *Hemoptysis* is present in a small proportion of cases. When due to intense pulmonary congestion, resulting from prolonged paroxysms of coughing or obstruction to the pulmonary veins, it is usually capillary in character, and appears at first either as streaks in the sputa or in moderate amount as clear,

bright-red blood, followed later by darker masses and small clots. When due to bronchial ulceration or erosion of a vessel in the wall of a glandular abscess, it is more profuse in character, appears suddenly, and may continue for several days, or even result in death.

4. *Pain* is one of the most frequent symptoms. In character it does not differ from that occurring with other forms of intrathoracic tumors. It has been described as dull and heavy, as a tightness or compression, and in a few cases has been spasmodic.

It is usually associated with some decided tenderness in pressure, and when once present is quite persistent, even when varying greatly in intensity.

It is most frequently located posteriorly between the spine and border of the scapula, opposite the bodies of the fourth, fifth, and, in a few cases, the sixth dorsal vertebræ. Less commonly it is felt in front, near the edge of the sternum, or under the clavicle, with occasionally a point of pain and tenderness in the axillary region, causing it to simulate intercostal neuralgia.

5. *Dyspnea* is often a prominent symptom. One fatal case is reported in which it was the only symptom. Its intensity depends less upon the absolute size of the tumor than upon the direction and nature of the enlargement. A comparatively small tumor or rapid inflammatory exudation may compress a primary bronchus sufficiently to cause most intense dyspnea.

When due to compression of a bronchial tube, or of the lung substance, the dyspnea is persistent and unvarying. In a small proportion of cases it appears to depend upon implication of the laryngeal nerve and unilateral paralysis of the larynx. It may be paroxysmal, or even assume the characteristics of spasmodic asthma with decided nocturnal paroxysms, and it is occasionally so severe as to force the patient to assume the erect position. Quain gives the proportion in which this spasmodic element is well marked as one in fifteen.

6. *Dysphagia* is a quite common symptom, and is due simply to compression. It is present in about fifteen per cent. of cases. It comes on slowly, is persistent, and varies only with the changes in the size of the glandular tumor. It is first noticed and most marked as regards solid food, but in one or two cases it was almost confined to liquids.

7. *Change of voice* is present only when the recurrent nerves are implicated. There may be loss in volume and force in connection with the dyspnea of bronchial obstruction, but distinct changes in character are probably always of nervous origin.

Hoarseness is the earlier and may be the only change. It occasionally passes into complete aphonia. In these cases paralysis of one or both vocal cords can be recognized.

8. *Nausea and vomiting* are rare symptoms, due to implication of the pneumogastrics. M. de Mussy considers them more frequent when the left nerve is affected.

9. *Venous Compression.*—Compression of the ascending veins seldom causes any marked symptoms. Anorexia and the general disturbances of digestion have only an indirect relation to venous obstruction.

Compression of the veins coming from the head is more frequent, causing cyanosis, congestion, and edema of the face and neck, and rarely of the upper extremities. Epistaxis results from the same cause.

Physical Signs.—*Inspection* is usually negative. It may show: 1. The edema, puffiness, etc., just mentioned of the face. 2. Slight prominence of the upper sternal and infraclavicular regions. This is exceedingly infrequent; it was noticed in none of sixty cases reported by Quain. 3. Slight flattening of the affected side. It is the more frequent change, and is probably induced by bronchial occlusion and partial pulmonary collapse. 4. Diminished motion of the affected side. It may be present alone or in connection with either enlargement or contraction. 5. No change in either size or motion. Most cases will be of this nature.

Palpation will show decreased vocal fremitus when bronchial compression has resulted in occlusion of the tubes.

Percussion.—Dulness is the most constant physical sign, and will indicate, by the area over which it is present, and by its character, both the size of the glandular enlargement and its nearness to the surface. It is usually best marked behind, between the scapula and spine, extending in extreme cases from the fourth to the sixth, or even seventh, dorsal vertebra. Less frequently it may be obtained in front, over the manubrium sterni, and below the sternal end of the clavicle.

Rarely pulmonary collapse causes partial dulness over a greater or lesser area. Abscess cavities communicating with the bronchial tubes are seldom, if ever, of sufficient size to affect the percussion note.

A compensatory emphysema may possibly give a vesiculo-tympanitic tone over the healthy lung.

Auscultation.—The respiratory sounds will be variously modified by the size of the tumor and its relations to the pulmonary tissue and bronchial tubes.

Weakness or entire absence of vesicular murmur is the more frequent change. It is due principally to bronchial obstruction, but in some cases is caused by direct compression of the pulmonary tissue. In the former case the change may be observed over a considerable area, or even an entire lung, but in the latter it will be more localized.

In an almost equal number of cases the respiratory sounds are loud and harsh, or even distinctly tubular. These changes are found only over the seat of the disease, and depend upon compression and closure of the alveoli and smaller tubes.

A venous hum, heard best at the root of the neck, and more common in children, is usually present when there is decided compression of the descending venous trunks.

Bilateral examination of the chest with the *x*-ray will often reveal a thoracic tumor and locate it on or about the bronchial tubes.

Diagnosis.—It is evident from the foregoing description that, in the earlier stages at least, a positive diagnosis is impossible. In no two cases will the symptoms or their order of development be alike.

They indicate only some form of intrathoracic growth, and may all be present with mediastinal tumors or thoracic aneurysm.

Mediastinal tumors are more frequently primary, those of the bronchial glands secondary.

Malignant growths are more common in the mediastinum, while inflammatory processes and tuberculous deposits more frequently affect the bronchial glands.

With mediastinal growths, especially of the anterior mediastinum, disturbances of circulation usually precede those of respiration, the contrary being the rule in disease of the bronchial glands.

Although both show a tendency to extend inward, mediastinal tumors are much more frequently attended by enlargement and bulging of the chest wall. Distinct physical signs can usually be obtained earlier in mediastinal than in glandular disease.

In thoracic aneurysm, also, the early symptoms are those connected with the circulation, while respiratory disturbances, both subjective and physical, are developed late. The arterial murmur, aneurysmal bruit, with a thrill and heaving impulse on palpation, is a valuable point of differentiation. In aneurysm the area of dulness increases along the course of the artery or rises into the neck, while in bronchial-gland enlargement it is more fixed, increases less laterally, and is more common behind than anteriorly. Diminution and delay of the radial pulse upon one side and

cardiac hypertrophy are occasional symptoms of thoracic aneurysm.

Erosion of the sternum, so frequent with aortic aneurysm, does not result from disease of the bronchial glands.

Prognosis.—The most important element in prognosis will always be the nature of the pathic process.

Malignant disease here, as elsewhere, terminates fatally, and tuberculosis will have a similar endings Syphilitic growths, simple enlargements of scrofulous origin, and subacute inflammatory processes may often be arrested and a practical cure effected when the nature of the disease can be recognized early. In such cases the size of the growth, the rapidity with which it is extending, and its relations to and effects upon adjacent tissue must form the basis of any prognosis. The more serious complications are those arising from implication of the laryngeal nerves and obstruction of the vessels. Glandular abscesses which open into bronchial tubes may be followed by recovery, but are more frequently fatal, either immediately or from prolonged suppuration and exhaustion.

Treatment.—The cases in which treatment has proved distinctly effective have been the chronic enlargements. The iodides, with iron and cod-liver oil internally, and counterirritation between the scapulæ, have been the most successful measures employed. The iron and iodine may be given separately or in combination. For syphilitic cases, in which large doses of iodide are required, the former method is to be preferred, but in non-specific cases the syrup of the iodide of iron may be given with equally good results.

In cases of the lymphatic diathesis or definite tuberculosis, treatment should be based on the demonstrated relation of lime assimilation to these conditions.

The persistent use of small (grain $\frac{1}{60}$ to $\frac{1}{40}$) doses of the bichloride of mercury has occasionallyd benefite some cases even when no syphilitic element was present, and this plan may be tried when the iodides are unavailing.

Counterirritation over the seat of the disease is always of decided value. It may be obtained by the use of any of the more persistent counterirritants, as the tincture of iodine, iodine liniment, blisters, or the actual cautery.

The special symptoms require palliative treatment.

The cough is seldom relieved by expectorants, and is best controlled by sedatives and antispasmodics. Codeine, heroine, morphine, and chloroform inhalations, in the spasmodic form, are the most certain in their effects, but the bromides, belladonna, Hoffman's anodyne, and chlorodyne are of value, and may suffice in some instances.

Pain is best relieved by anodyne lotions, and when severe by hypodermics of morphine. For local applications, laudanum, belladonna, chloroform, or camphorated liniments may be employed.

Dyspnea is more safely relieved by chloroform inhalations and the ethereal preparations than by opium or other narcotics.

The enforcement of general hygienic and tonic measures will greatly increase the efficacy of any form of treatment. Charles E. Quimby.

Bronchiectasis.—Dilatations of the bronchi, either diffuse or circumscribed, are known as bronchiectases. They are of common occurrence and arise from a great variety of causes. In all cases, however, the essential cause of bronchial dilatation is to be found in a weakness of the bronchial wall or an increase of pressure within the bronchus, or in a combination of both these factors. Bronchiectases appear both clinically and pathologically in such a variety of forms that their classification is difficult. According to their etiology they may be divided into the following forms: 1. Congenital, 2. Atelectatic, 3. Vicarious, 4. Emphysematous, 5. Inflammatory.

General Morbid Anatomy. The condition of bronchial dilatation may be single or multiple, one or more of the bronchi being affected. In some cases the entire bronchial tree is dilated (*universal bronchiectasis*). When but one bronchus is dilated the condition is usually found in the upper lobes; when many are dilated the lower lobes are affected. Usually the bronchial branches of the third or fourth order are the ones involved; they not infrequently become wider than the main bronchi, and may often be followed out

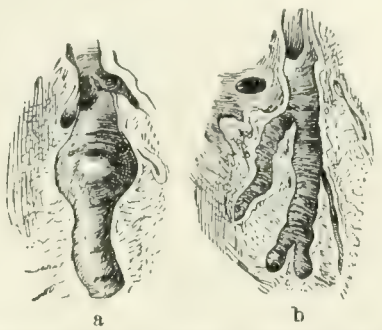


Fig. 1111. Saccular and Cylindrical Forms of Bronchiectasis. (After Orth.) *a* Saccular form; *b*, cylindrical form.

to the pleura, where they end generally in a sac-like terminal dilatation of somewhat greater width, as is seen in Fig. 5130, *b*). In other cases the terminations may be of normal width, or they may become narrowed. The smaller bronchi may at times alone be dilated, the lung on section resembling a very porous cheese ("cheese-lung," "turtle-lung").

The dilatation may be more or less uniform (*cylindrical, fusiform,* or *spindle-shaped bronchiectasis*), or it may be localized, the dilatation being much greater at one point than elsewhere, or involving but a small portion of the bronchus (*saccular bronchiectasis*). In other cases a succession of dilated portions may be separated from each other by portions of the bronchus which are of normal width or are constricted (*varicose, moniliform,* or *rosary bronchiectasis*). The different forms may be found in the same lung. The cylindrical variety is usually diffuse, the saccular circumscribed. Pathological changes in the bronchial wall are always present in the latter form. Closure of the central end of the dilated portion and the accumulation of secretions may give the dilatation the character of a cyst (*bronchiectatic cyst, cystic bronchiectasis*). Suppuration of the wall of the dilated bronchus gives rise to the conditions known as *ulcerative bronchiectasis* and *bronchiectatic abscess.* Enlargement of the bronchiectasis at the expense of the surrounding lung tissue leads to the formation of bronchiectatic cavities (*cavernous bronchiectasis*). Infection of the dilated bronchus with putrefactive organisms causes a *gangrenous bronchiectasis.* In this case also the destruction of the wall of the dilatation and the encroachment upon the surrounding tissue give rise to the formation of cavities. In some cases the larger bronchi may be chiefly affected, in which event the distended portions project from the main bronchus like the dilated fingers of a glove. The size and number of the dilatations vary greatly. They may be microscopic or as large as an orange, but as a rule are one to two centimeters in diameter. When large, the number is usually small.

The walls of the dilated portion may appear to be normal, or they may show marked pathological

changes. The inner lining may be smooth and shining, or roughened, and is usually more or less reddened. The smooth-walled dilatations often contain no fluid. As a rule the bronchial mucosa presents the appearances of a chronic purulent catarrh. The cylindrical epithelium is usually replaced by one of a cubical or squamous type. In the large saccular bronchiectases and in some of the cylindrical forms due to retained secretions the lining membrane may be ulcerated. Polypoid outgrowths are not infrequently seen. The contents of the cavity may be thin and watery, or thick or even caseous. When the outlet is obstructed the contents may be inspissated and chalky, or converted into firmer masses (broncholiths). In some of the larger bronchiectases, and particularly in the case of secondary gangrene, the contents are horribly fetid. Microscopically the fluid consists of mucus, pus corpuscles, desquamated epithelial cells, fatty acid crystals, and occasionally blood and hematoidin crystals. In the case of ulcerative or gangrenous conditions of the walls elastic fibers may also be present. The outer portions of the wall of the dilated portion may be markedly atrophic; even the cartilage plates may entirely disappear. The elastic tissue is stretched and separated; and the muscle, if it has not entirely disappeared, is much stretched and atrophied. In the middle portion of the dilatation the muscle fibers are usually wholly lost. The mucous glands may also entirely disappear, or may show extreme mucous degeneration. In other cases a secondary thickening of the wall, due to a new formation of connective tissue and elastic fibers, may occur. This is true particularly of the inflammatory cases. Small-celled infiltration of the wall is usually present. According to the condition of the bronchial wall bronchiectases may be divided into the *atrophic* and the *hypertrophic* forms. Such a classification has, however, but little practical importance, inasmuch as both forms may be found in the same lung. In general, the condition of the wall is dependent essentially upon the cause of the dilatation.

Fig. 1145.—Atrophic Cyclindrical Bronchiectasis with Ribbed Transverse Markings. (After Ziegler.)

The *atrophic form* occurs in association with emphysema, and as a sequela of old chronic inflammatory processes which lessen the elasticity and resisting power of the bronchial wall, so that it gives way to the air pressure. Prolonged and difficult expiration favors its occurrence. Such dilatations are usually cylindrical and occur chiefly in the bronchi of the lower lobes. Very often the stretching of the bronchial wall is not uniform, and the inner surface shows circular or oblique ribbed elevations corresponding to circular bands of muscle fibers and elastic tissue which are still preserved, the connective tissue between them being pushed outward. All the elements of the wall are more or less atrophic, even the cartilage, which may be replaced by connective tissue containing newly formed blood-vessels. The openings of the mucous glands are dilated and funnel-shaped. The epithelium may be well preserved, or it may be changed to a cubical or flattened variety, or may be desquamated. In dilatations of long standing it has usually disappeared.

The *hypertrophic* form occurs as a frequent sequela of indurations and contractions of the lung parenchyma. In these cases the greater part of the lung is usually impermeable to air, and the cause of the dilatation is less a result of the weakening of the bronchial wall, but is essentially dependent upon an increase of intrabronchial pressure, which is due to the fact that the air entering the bronchi no longer passes normally into the ramifications of the air passages. In the case of retraction of the lung tissue with pleural adhesions the outward pull upon the bronchial walls is also an important factor in causing a dilatation of the bronchial lumen. In both cases the dilatation is favored by any inflammatory process which weakens the wall. The mucous membrane of the dilated bronchus in the hypertrophic mass may resemble that found in the atrophic forms, or papillary or polypoid proliferations may be present. A lattice-like marking of the lining

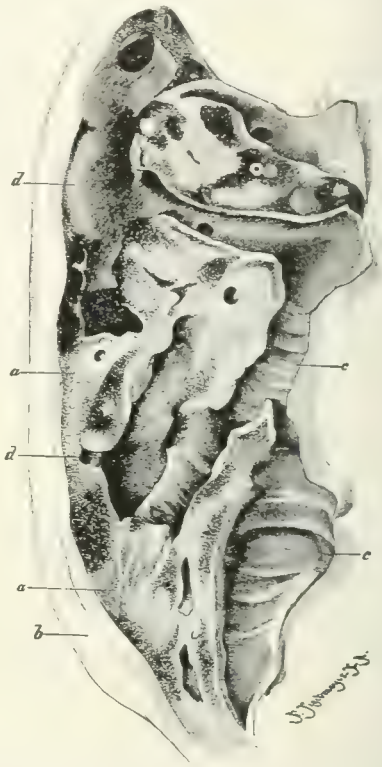


Fig. 1146.—Hypertrophic Bronchiectasis and Bronchiectatic Caverns in Fibroid Induration of Lung. (After Ziegler.) *a*, Indurated lung-tissue; *b*, thickened pleura; *c*, dilated bronchus; *d*, cavity communicating with a dilated bronchus.

membrane is often seen. These markings correspond to small thickenings or elevations of the mucosa corresponding to the formation of a very cellular granulation tissue about the longitudinal and transverse bundles of elastic tissue. The connective tissue of the wall and of the peribronchial region is more or less thickened, and connective tissue may take the place of the mucous glands and cartilages. The capillaries of the wall are greatly dilated (sacculated aneurysms) and present thickened walls. The hyperemia of the wall may be so marked that the appearance of the mucosa suggests a hemorrhagic condition and hemorrhage from these dilated capillaries is not uncommon. Tuberculous and gangrenous processes may cause various modifications of these appearances.

The *saccular* bronchiectases usually develop at the cost of the lung parenchyma. The bronchus may show at some point in its course a dilatation varying in size from that of a mustard seed to that of a hen's egg, or the bronchus may terminate in a sac. The central end of the dilatation may become obliterated and the dilatation thus come to resemble a cyst. Through the accumulation of secretions the cyst may attain great dimensions. All of the bronchi of one lung may be similarly affected, the lung tissue between

becoming atrophic and compressed, so that the organ finally comes to resemble a multilocular cyst. In other cases the saccular dilatation may involve only a portion of the circumference of the wall, so that it appears as a diverticulum which is connected with the lumen of the bronchus by a narrow opening only (*dilatation ampullaire latérale* of Cruveilhier). In the majority of cases the saccular dilatations involve the smaller bronchi; more rarely are the main branches affected. They are usually associated with bronchial stenoses, and are most often found near the periphery of the lung. According to Gairdner all of the saccular dilatations are the result of ulcerative excavations of the lung tissue. This is true, however, of only a part of the cases.

Biermer divides bronchiectases, according to the character of their walls, into the following forms: (1) Dilatations with catarrhal swelling and relaxation of the bronchial wall. These are acute and occur chiefly in the lungs of children affected with chronic bronchitis. After the bronchitis has been cured the bronchial wall regains its old tone and elasticity, and the dilatation disappears. (2) Dilatations with hypertrophic walls. These affect the larger bronchi and are usually spindle-shaped. (3) Dilatations with thin walls. These are usually saccular. (4) Dilatations with trabecular degeneration. The walls are uneven, thickened, and there is a peribronchial increase of connective tissue.

Ulcerative processes are of common occurrence in the mucosa of the saccular bronchiectases. Complete destruction of the elements of the wall may take place, giving rise to a bronchial abscess. Infection with putrefactive bacteria leads to a secondary gangrene. Such changes are due to the lessened resistance of the bronchial walls, the changes in the secretions, and the entrance of bacteria. In these cases elastic tissue may be found in the sputum. Deposits of lime salts may occur in the bronchial walls, and as the result of the formation of granulating surfaces adhesions of the walls or the development of connective-tissue bridges may take place. In some cases a complete obliteration of the lumen results, and the bronchus is converted at the point of dilatation into a fibrous cord

Changes in Lungs and Pleura.—Chronic inflammation is always present in the bronchiectatic lung, corresponding usually in degree to the duration and extent of the bronchial affection. Either lobar or lobular pneumonia may precede the dilatation. Fibrosis is present in a large number of cases. Pleurisy with effusion, and especially empyema are often associated with bronchiectasis. The changes in the lung tissue in the neighborhood of the bronchiectasis are usually primary, with the exception of ulcerative and gangrenous processes, which are secondary to the dilatation. The bronchi which are not dilated show catarrah and a putrid decomposition of the secretions. They are often wholly obliterated. In bronchiectases due to syphilitic affections of the air passages the dilatation of the smaller bronchi is usually secondary to a stenosis of the trachea or large bronchus. The portions of the lungs not affected by the condition causing the bronchiectasis may present a compensatory emphysema, and in the later stages foci of bronchopneumonia, due to the aspiration of secretions from the dilated bronchi, may be found. The right ventricle may become hypertrophied and dilated as the result of the stasis in the pulmonary circulation. The bronchial glands are usually swollen, and may suppurate.

Metastasis may take place from bronchiectases. Biermer observed metastatic brain abscesses in four cases of bronchiectasis; and Gerhardt and Bardenheuer noted the occurrence of rheumatic joint affections in patients with bronchiectases. Chiari has reported a case of suppurative myelitis following bronchiectasis. In the pus and vessels of the cord a branching filamentous fungus was found which showed threads breaking up into coccoid bodies and staining with Gram's mixture. Of eight cases of hematogenous myelitis collected from the literature three were secondary to bronchiectasis. In one case of actinomycotic abscesses occurring in the brain of a man with numerous bronchiectatic cavities, many clusters of the fungus were found in the walls and contents of the latter.

Location.—Statistics as to the location of bronchiectases are of doubtful value. This is particularly true with regard to the relative frequency of involvement of the right and left sides and the upper and lower lobes. The statements generally made in regard to these points are to the effect that bronchiectases usually occur in one lung, and more frequently on the left than on the right side, and more often in the upper lobe than in the lower, and that in double-sided bronchiectasis both upper lobes are more often affected than the lower ones. But little importance can at present be attached to such statements, the number of observations upon which they are based being too small. The dilatations occurring with tuberculosis and chronic inflammatory processes are more often seen in the upper lobes; in the case of pleuritic exudations in the compressed lower lobes; those occurring as sequelæ of croupous and catarrhal pneumonia, hypostatic and atelectatic conditions are found in the lower and posterior portions. In the case of pleural adhesions the dilatations are sometimes found in the bronchi of the upper lobe, sometimes in those of the lower lobe.

Etiology.—This is varied, and the cause and pathogenesis of many cases are obscure. It is generally agreed that dilatation cannot take place in a healthy bronchus, but that some pathological condition must first weaken its walls: acute, subacute or chronic bronchopneumonia, unresolved lobar and lobular pneumonias, foreign-body in a bronchus, chronic influenza, whooping-cough, bronchial stenosis, atelectasis, fibrosis of lung, chronic pleuritis, trauma, tuberculosis, syphilis, neoplasm, and aneurysm are the most frequent causes. Much interest attaches to the recent reports of bronchiectasis due to deep infection of the bronchial walls with influenza bacilli. Some cases are congenital, due to disturbed development. No age is exempt, although bronchiectasis is rare in infants. It is frequent in children after the age of three, and in adolescents. Men are more frequently affected than women.

Congenital Bronchiectasis.—Under this head there is included a number of conditions in the lungs of the new-born which have been regarded as due to congenital syphilis. One lung (most often the left) is usually affected; it may contain numerous cysts filled with a serous fluid. The lung tissue between the cysts may be indurated or atelectatic. Heller, Herzheimer, Grawitz, and others have described cases which, according to Grawitz, are to be ascribed to an hydropic dilatation of the bronchi. Heller regards them as representing the bronchi of undeveloped portions of the lung, the dilatation occurring in later life partly as the result of the growth of the thorax and the consequent pull upon the bronchus, and partly as the result of the growth of the bronchus itself and the pressure of retained secretions. Accessory lobes ("accessory lungs") are occasionally found. They may not communicate with the main bronchial tree, but may contain bronchiectases in the form of cysts. They are most frequently found between the esophagus, spinal column, and diaphragm. The cases of unilateral atrophy of the lung (left) described by Neisser are probably the result of congenital bronchiectasis. In all the cases there were intermittent attacks of cough, dyspnea, fever, and putrid or bloody sputum from childhood. Atrophy of left lung, compensatory hypertrophy of the right,

displacement of the heart to the left, and high diaphragm without retraction of left thorax characterized the cases. Ogle has reported a case of bronchiectasis associated with a dermoid cyst.

Atelectatic Bronchiectasis.—The congenital bronchiectasis of Heller is to be placed in this class. In a number of cases observed bronchial dilatations have been found in adults, the lung tissue being free from pigment and showing no evidences of inflammatory changes. The condition is therefore very probably the result of a congenital atelectasis. An acquired bronchiectasis, due to atelectasis, may take place in later life as the result of deformities of the thorax, tumors, aneurysm, etc.

Vicarious Bronchiectasis.—If the entrance of air into any portion of the lung be hindered and the volume of that part reduced, the inspiratory pull upon the sound portions of the lung is increased. As the result of this increased pull both the alveoli and the bronchi become dilated, and there arise a vicarious emphysema and a vicarious bronchiectasis. Pneumonic foci, infarcts, local atelectasis, local tuberculous nodules and infiltrations, contracting scar tissue, etc., are the causal factors of such bronchial dilatations. The bronchial wall and mucosa become stretched and thinned like a serous membrane. The essential characteristic of the change is that no inflammatory processes take part in the direct production of the dilatation. It is to be regarded as a vicarious emphysema of the bronchi. The clinical significance of the condition is not great. The dilatations are relatively small and circumscribed. Inflammatory changes may follow, and an ulcerative or inflammatory bronchiectasis develop.

Emphysematous Bronchiectasis.—An emphysema of the bronchi occurs also in simple atrophic emphysema of the lungs not due to a compensation for portions of the lung the function of which is lost or diminished. It is to be regarded as idiopathic rather than vicarious or compensating. The dilatation is not great, but the walls of the bronchi are greatly thinned. The smaller branches, particularly those of the lower lobes, are chiefly affected. The symptoms cannot be separated from those of alveolar emphysema.

Inflammatory Bronchiectasis.—This is by far the most common and important form. All authorities are agreed that for the production of a bronchiectasis of clinical importance an inflammatory weakening of the bronchial wall is necessary. In general there are no severe inflammatory conditions of the lungs or pleura in which bronchiectases may not develop. Capillary bronchitis, chronic bronchitis, catarrhal pneumonia, croupous pneumonia, particularly when running a subacute or chronic course, influenza, tuberculosis, obliteration of the bronchioles due to indurations, peribronchitis, typhoid hypostasis, stenosis of the large bronchi, pleuritis, pleural adhesions, etc., are the causal and predisposing factors. General anemia, marasmus, alcoholism, excessive or forced respiratory movements, singing, screaming, coughing, etc., play a secondary part. In the case of bronchial stenoses the bronchus is usually dilated both above and below the point of stenosis. It is probable that the dilatation which lies below the stenosis is due to the fact that the air which passes through the stenosis into the portion of the bronchus below it is held there by the blocking of the stenosis with mucus during expiration, and as the result of the expiratory increase of pressure this portion of the bronchus becomes stretched. In the case of foreign bodies the bronchial dilatation is found not only around the body, but involving other bronchial branches as well. The causes of such dilatations are complicated, but the essential factor is the production of a peribronchitis. Tuberculosis and syphilis may give rise to bronchiectases which are primarily dependent upon stenoses caused by the contraction of scar tissue, or are due to infiltrations. Primary carcinoma of the lung or large bronchi also frequently causes bronchiectasis as the result of bronchial stenosis. Chronic pneumonia, whether following the acute pneumonias, or due to syphilis, pleuritis, foreign bodies, etc., or primary of unknown origin, is of especial importance in the etiology of bronchiectasis.

Symptoms.—*Cough* is the rule. It occurs in paroxysms, usually at long intervals, almost always on the patient's awakening in the morning, the paroxysm being repeated once or several times during the day. The patient may be awakened by the first paroxysm, or it may come on after arising. Usually the patients know the time when the attacks may be expected. A paroxysm may also be precipitated by the patient's lying upon the affected side and then turning suddenly into another position. The attacks are often very violent and convulsive, at times completely depriving the patient of breath. The frequency and severity of the cough are dependent upon the position and the character of the opening of the dilatation. As long as the secretions are retained within the cavity there is no coughing, but when these escape into the neighboring bronchi and alveoli paroxysms are excited. When the bronchiectasis is located in the apex the secretions may pass continuously into a vertical bronchus and thus give rise to almost constant coughing.

Dyspnea.—This may be slight or entirely absent; it usually increases in degree toward the later stages of the affection and may become very marked. Ordinarily it is noticed only at the time of coughing, or after vigorous exercise. It is increased in the event of acute catarrhs of the respiratory tract, and in the case of the collection of mucus in the smaller bronchi. Persistent dyspnea is due to some complication on the part of the heart or lungs.

Expectoration.—The attacks of coughing are attended by expectoration. This may resemble that of any ordinary bronchitis, but in the majority of cases the expectoration is very characteristic and of diagnostic importance. With the coughing paroxysm there is a gush of sputum so great as to fill the patient's mouth. Within a few minutes an ordinary sputum cup may be entirely filled. The total amount of sputum may be so great as to suggest the possibility of the perforation of an empyema into the bronchus or lung. One-half to one liter (one to two pints) may be expectorated within the twenty-four hours. With the evacuation of the dilatation the coughing usually ceases, to begin again as soon as the bronchiectasis fills up. Usually the sputum is raised easily, without much effort or coughing, but in the case of such complications as pleuritis, emphysema, tracheal or bronchial stenosis, etc., the expectoration may be very difficult. Nausea and vomiting are rarely produced. The position of the patient is of great importance; when he lies upon one side there may be neither cough nor expectoration, but as soon as he turns upon the other side the bronchiectasis begins to empty itself and the cough and expectoration are excited. Sensations of pressure, fulness, and pain are sometimes felt before the expectoration takes place, particularly in the case of children. Occasionally these symptoms may be very marked, lasting half an hour or so before the expectoration occurs. The large amounts of sputum and the long periods between the attacks of expectoration may be explained as due to a lessened irritability on the part of the bronchial mucosa, a larger quantity of sputum being necessary to excite coughing. The amount of sputum raised is always greater during the morning hours. Toward the end of the affection the total amount decreases as the patient becomes weaker.

Sputum.—The sputum is usually purulent in character, but may be fetid or gangrenous. When purulent it is yellowish and contains more or less mucus. If fetid in character the odor may be extremely disagreeable and penetrating, so that the patient's

breath may be perceived some distance away. The patient himself shows a remarkable tolerance of the odor; nausea is rarely produced. In the gangrenous cases the sputum is grayish-yellow or greenish in color. When the complication of gangrene is not present the sputum may have no putrid odor, but commonly possesses a disagreeable, nauseating, acid, or sweetish smell (pseudogangrene). When collected in a glass or cylinder the sputum separates into two distinct layers: an upper, thin, slightly cloudy, almost serous layer; and a lower, thick, purulent layer containing caseous masses. The latter appear as dirty yellow plugs varying in size from a mustard seed to a bean (plugs of Traube or Dittrich). If the sputum be put into a tall cylinder which is half filled with water, four distinct layers may be seen. The uppermost is foamy; the one beneath this consists of muco-purulent masses, which hang down in the form of shreds into the third layer, consisting of cloudy water. The lowest layer of water has a grayish-green appearance.

Microscopically the sputum is made up of pus corpuscles which may be well preserved or contain fat droplets. In the case of putrid decomposition bacteria, crystals of fatty acids, margarin, tyrosin, leucin, and triple phosphates may be present. Blood-pigment may also be found. In the case of gangrene elastic fibers may be present. The caseous plugs stain a brownish-yellow, blue, or violet with dilute iodine solutions. The mucin content of the sputum varies greatly. Blood-cells are not infrequently present, particularly in the late stages.

Hemorrhage.—The presence of blood in the sputum of bronchiectasis is not rare. The amount is usually small, but the hemorrhage may be so large or so frequently repeated that severe symptoms or even death may ensue. The sputum in such cases may appear to be chiefly blood; it is rarely bright-red, but is more or less discolored by the mixture with the other elements of the sputum. The smaller hemorrhages are chiefly of capillary origin; the large ones come from the erosion of large vessels in the wall of the dilatation. In ulcerative conditions of the wall the hemorrhages may be very severe, persist for a long time, and finally lead to death.

General Symptoms.—When secondary changes in the heart, kidneys, etc., are not present, the general condition of the patient may be quite good or fair. Fever and sweating are signs of complications. Occasionally fever may be caused by the absorption of products of decomposition from the cavity. In such cases the fever does not present any distinct type. Pain, when present, is not caused by the bronchiectasis, but is pleuritic in character. Some cases of bronchiectasis run without any symptoms whatever.

Physical Signs.—The physical signs in bronchiectasis are not characteristic, inasmuch as all of them may occur in other diseases of the lungs.

Inspection.—The color of the skin is usually unchanged. When it is very pale the underlying disease is most likely to be tuberculosis; when it is cyanotic there is usually emphysema present. Many of the patients lie upon their backs; others sit bending forward, claiming that this prevents the swallowing of the sputum. When the bronchiectasis is confined to one side, the patients usually lie upon the affected side, coughing and profuse expectoration being caused by turning upon the sound side. Deformities of the thorax are rare, occurring only in the case of retraction of the lung, or when extensive pleuritic adhesions are associated with the bronchiectasis. Diffuse or localized retraction of the thoracic wall and curvature of the spine may result from these conditions. When emphysema is present the thorax may present the characteristic barrel form. Occasionally differences of movement may be made out between the two sides. In the case of extensive bronchiectases of the lower lobe of one side there may be seen during deep inspiration a wave-like retraction of the intercostal spaces proceeding from above downward. On the affected side such a movement is not visible. A compensatory emphysema of the sound lung is always found in such cases. Very rarely it may be seen that the respiratory movements on the affected side lessen, and at last wholly cease as the bronchiectasis fills up, but return after the expectoration has emptied the bronchus.

Among the most common and important of the physical signs of bronchiectasis are the changes which take place in the distal phalanges of the hands and feet (drumstick fingers). The clubbing of the fingers is due to an hypertrophy of the terminal portions of the bones (*ostéoarthropathie hypertrophiante pneumique*), so that the joints of the phalanges, the carpal joints, and even the wrist joint may be greatly thickened. These changes take place in association with chronic cyanosis and appear to be dependent upon the latter. They are also found in other conditions than bronchiectasis, particularly in the congenital heart lesions; but Bamberger has attempted to show that the change in bronchiectasis is characteristic of this affection, in that it is a painful hypertrophy of the epiphyses.

Palpation.—Vocal fremitus is increased over areas of fibrosis.

Percussion.—The percussion phenomena of bronchiectasis vary greatly, being dependent upon the size of the dilatation, the quantity of fluid present in it, its distance from the chest wall, and the character of the changes in the surrounding lung tissue. Dulness or a tympanitic tone may be obtained, or both alternately, according as the cavity contains fluid or air. A tympanitic tone with change of pitch on opening and closing the mouth may be noted, as well as change of tone on change of position, the cracked-pot sound, metallic tones, etc., according to the conditions present. About the areas showing such signs of cavity the tone may be resonant; in the case of tuberculous cavities it is always dull. The dislocation of the neighboring organs, pleuritic thickenings, adhesion, etc., may also be shown by percussion.

Auscultation.—The vesicular murmur is weakened or absent, being replaced by a bronchial blowing. The cylindrical dilatations give a soft bronchial sound, and when containing fluid they yield also moist, coarse, bubbling râles. The saccular dilatations give both the percussion and auscultation signs of a cavity, particularly large, moist, bubbling râles. Gurgling sounds are common. "Skoda's veiled puff" is often present. There may be marked bronchophony and pectoriloquy. Râles may be produced by the heart movements.

Complications.—The most frequent and dangerous complication is the putrid or gangrenous decomposition of the contents of the dilatation. Pleuritis, peribronchitis, bronchopneumonia, chronic pneumonia, chronic bronchitis, lobar pneumonia, emphysema, chronic laryngitis, renal and cardiac affections, dropsy, albuminuria, cirrhosis of the liver, etc., may be associated with bronchiectasis or appear as sequelæ. Metastatic abscesses may occur in the brain, spinal cord, etc.; there may also be rheumatic joint affections. There arises in these cases a suspicion of the occurrence of a general pyemic infection. Perforation of the dilatation into the pleural cavity leads to the development of a pyopneumothorax. Perforation into the trachea or esophagus may occur, or very rarely into the pericardial sac. Primary carcinoma of the bronchus is usually associated with bronchiectasis, whether primary or secondary to the latter cannot usually be decided, and views differ as to the etiological relationship of the two conditions. In old chronic cases of long duration amyloid degeneration of liver, spleen, and kidneys may be found. Tuberculosis is a

fairly common complication. The heart is usually affected, hypertrophy and dilatation of the right ventricle occurring in the majority of cases. The cardiac changes are due partly to disturbances in the pulmonary circulation, partly to the accompanying condition of chronic intoxication, partly to local changes in the thorax, and partly to coincident renal changes.

Duration and Course.—Bronchiectases may remain stationary for years, the only symptoms being those of a chronic bronchitis. As a rule the dilatation gradually increases during this time without an increase in the symptoms. With the advent of fresh catarrhs emphysema gradually develops, the shortness of breath becomes more marked, and the patient may become cyanotic. The right heart becomes hypertrophic and finally dilated. Putrid bronchitis and gangrene may occur; from these the patient may recover for a time, or death may take place. As a rule the condition runs for a long time; amyloid disease of the kidneys may finally result and the patient becomes dropsical. After alternating periods of improvement and exacerbation, extending over a long period, the disease is brought to an end by some one of the complications, the most frequent being hemoptysis, pneumonia, gangrene of the lung, pyopneumothorax, pyemia, metastatic abscess of brain, and cardiac insufficiency following fibrosis of the lungs.

Diagnosis.—The differential diagnosis of bronchiectasis from other pathological conditions of the lung is sometimes very difficult. The absence of the tubercle bacillus will distinguish it from tuberculosis. When the latter process is combined with bronchiectasis the character of the sputum, the age of the patient, position of the cavity, habitus, etc., are points to be considered in the differential diagnosis. The history of the case is of greatest importance. It may be taken as a guiding principle that tuberculosis may lead to a bronchiectasis, but that a bronchiectasis rarely becomes tuberculous. Actinomycotic cavities may be distinguished by the presence of the fungus in the sputum. The rare localization in the lung of hydatids may also be easily diagnosed by the findings in the sputum. From pulmonary gangrene, abscess, putrid bronchitis, interstitial pneumonia, pyopneumothorax, etc., the differentiation is often impossible. The physical signs of cavity are of the greatest importance in so far as the differentiation between processes with cavity formation and those without is concerned. Much was expected from the use of *x*-rays in the diagnosis of bronchiectasis, but these expectations have not been realized. Only in the case of extensive peribronchial thickenings may aid be looked for by the use of *x*-rays. Only in one case (Pfeiffer) has a diagnosis of bronchiectasis been made by means of Röntgen plates and confirmed by autopsy. Very little aid can be expected from bronchoscopy.

Treatment.—In very rare cases self-healing of the bronchiectasis may take place. In children this may follow the cure of catarrhal bronchitis and the restoration of normal conditions of pressure. In extremely rare cases the bronchial cavity may be obliterated by adhesion of the walls of the cavity or through the formation of granulation tissue. Since in the great majority of cases such healing is impossible, the prophylactic treatment becomes of prime importance. The conditions (pleuritis, pneumonia, etc.) which lead to bronchiectasis should be appropriately treated with a view to the prevention of such dilatations. After the development of bronchiectases the chief therapeutic indication is to keep the contents of the dilatation —so far as lies in our power—aseptic. This can be perfectly accomplished only by residence in an atmosphere containing no bacteria. Removal of the patient to a suitable climate (California, Egypt) is the best means of avoiding the various complications of the affection. When this cannot be done the treatment becomes chiefly symptomatic and largely directed to antiseptic procedures. Inhalations of creosote, turpentine, menthol, eucalyptus, etc., and creosote vapor baths are recommended for this purpose. A number of writers speak favorably of the creosote vapor baths. These are, however, unpleasant and slow in operation, and do not always succeed in lessening the amount of the sputum. The crude creosote appears to be more effective than the various substitutes (vapo-cresoline, refined creosote, soluble cresol, etc.) which have been advised. Other writers have found success with guaiacol vapor baths after failing with creosote. The ordinary methods of giving such inhalations may, however, be a source of infection, as many of the forms of inhalation apparatus used are dirt traps.

Intralaryngeal or *intratracheal injections* of menthol, guaiacol, eucalyptol, iodoform emulsion, etc., have been advised by Rosenberg, Stewart, Campbell, and others, but are condemned by various writers because they give rise to constitutional disturbances, fever, and violent cough. Mendel advises the use of a five to ten per cent. eucalyptol in olive oil given in 3 c.c. doses three times daily for a month, according to the following method. The patient's tongue is held outside his mouth while the liquid is projected against the pharyngeal wall. If the patient refrains from swallowing while the tongue is protruded some of the fluid will run down into the air passages. The treatment should be interrupted and continued according to the patient's condition. It is said to be effective and easily carried out.

Subcutaneous injections of guaiacol (1 in 5) and creosote (1 in 5) in olive oil have also been recommended. They may give rise to inflammation and necrosis at the point of injection.

Intravenous injections of formalin (25 to 50 c.c. of a 1–2,000 solution of formalin in decinormal salt solution) have also been tried without success.

Injections of carbolic acid and menthol directly into the bronchiectatic cavity have also been attempted.

Murphy's method of filling the pleural cavity with air or nitrogen to such an extent as to cause a collapse of the bronchial cavity has been tried with some success. The air should of course be thoroughly sterilized. About 170 c.c. of air or nitrogen are injected every second or third day.

Inhalations of oxygen may aid in reducing the odor of the sputum. Symptomatic treatment with expectorants (apomorphine, senega, ipecacuanha, etc.) may at times give relief or temporary improvement. Hemorrhage should receive appropriate treatment.

Inasmuch as the medical treatment is usually without avail, much has been hoped from surgical intervention in the treatment of bronchiectasis. This has now been given a very extensive trial, with complete failure in the majority of cases, and partial success in the others. These unsatisfactory results are easily understood when we consider the facts that the dilatations are often multiple and bilateral, and that the pulmonary tissue is usually extensively diseased. Dangerous hemorrhages may result, and anesthesia is in itself attended with danger in these cases. The uncertainty of the physical signs also contributes to the unsatisfactory results. Operation is indicated in the case of circumscribed saccular bronchiectasis when the other lung is sound. Extensive extrapleural resection of the ribs, three to four centimeter pieces being removed from the first to eighth ribs at the costal angle, is practised to secure complete collapse of the affected lung. The results have not been very satisfactory. Tuffier has transplanted omentum and lipomas between the pleura and chest wall to bring pressure upon the cavities in the lungs. Numerous animal experiments have been carried out with reference to the securing of a collapse of the lung after

ligature of the pulmonary artery or vein of the affected lobe. Application of these methods in the human body has not yet been made.

In opposition to these methods a number of operations made directly upon the cavity have been tried out with some success. Pneumotomy, the slitting of the dilated bronchus, is the one operation that has been given the most extensive trial. It demands the existence of pleural adhesions to prevent danger of infection for its successful carrying out. It is performed in many ways. Sixty-two per cent. of the cases operated upon to date died from the operation or subsequent complications; in 9.4 per cent. alone was healing obtained.

Better results have been obtained by pulmonary resection, removing the entire diseased portion. Cases of successful resection with healing have been reported by Lenhartz, Gluck, Körte, Krause, Kümmell, Sauerbruch and others. Their success is in marked contrast to that of the other methods mentioned above, and promises well for the future development of this method. Still more radical is the extirpation of the entire diseased lobe or even lung. After much animal experimentation extirpation of a lobe or entire lung has been performed in man by Friedrich, Garré, Körte, Gluck, Kümmell, Müller, Tiegel, Danielsen and others, not only for bronchiectasis but also for tuberculosis and carcinoma. The chief dangers of pulmonary surgery, severe disturbances of respiration, pneumothorax, sudden collapse, etc., are combated by various forms of apparatus for the regulation of pressures. For a résumé of the surgical treatment of bronchiectasis, with literature, see Batzdorff (*Centralblatt. f. d. Grenzgebiete d. Medizin u. Chirurgie*, November, 1912).

The *postural* treatment of bronchiectasis is strongly recommended by Ewart (*Lancet*, 1901). While not regarding it as curative in advanced cases, he holds that no other treatment is so simple, so rational, and so effective. In a case so treated the relief afforded the patient was striking; the persistent pyrexia stopped, and the gushing character of the expectoration ceased. Ewart advises a continuous elevation of the foot of the bed of from twelve to fourteen inches. For brief periods a greater elevation may be employed with benefit.

Prognosis.—In so far as a cure is concerned the prognosis in any well-established case of bronchiectasis is bad. Except in rare cases no method of treatment at present employed is of avail in effecting a cure. Some of the more acute cases in young persons may, however, be cured. In the chronic cases our present methods of treatment can only relieve the distress of the affection and prolong life; but from the development of pulmonary surgery and the improvement of technical methods we may look forward with hope to an improvement in the prognosis of bronchiectasis. Aldred Scott Warthin.

Bronchitis.—Acute bronchitis, chronic bronchitis, and fibrinous bronchitis will be discussed under this heading.

Acute bronchitis may be an affection involving only the larger and medium-sized tubes or the process may extend to the finest subdivisions of the bronchi. Processes involving the larger tubes constitute the mild form, those involving the smaller tubes the severe form. Capillary bronchitis which is always accompanied by involvement of the lung is more properly classed as bronchopneumonia (*q.v.*).

Beginning suddenly with a sense of constriction beneath the sternum and a dry unproductive cough, or more gradually as an extension from a pre-existing laryngitis, the patient afflicted with bronchitis of the larger tubes in a few days develops a productive cough as diminution of the distress and in a week is well on the way to recovery. In adults the temperature may be slightly elevated for a day or two. In children the temperature is higher and more prolonged, frequently persisting for a week. Acute bronchitis of the smaller tubes on the other hand is a more serious affection. The temperature range is higher, the course is longer, the cough more severe, and the end results more grave.

Etiology.—A convenient classification of the causes of bronchitis is one that divides them into specific and non-specific. The specific class includes those cases developing at the beginning or during the course of some special disease as influenza, typhoid fever, syphilis, etc. The non-specific class includes cases of bronchitis from all other causes as gaseous, thermal, mechanical, possibly bacteriological, and those originating within the body, as in cardiac affections, gout, and nephritis. The inhalation of irritating gases or fumes or fine dust is a potent cause of bronchitis, and its action is readily understood. Elimination of toxic substances, as iodides, may cause bronchitis. Deformities of the nose and the presence of adenoids and enlarged tonsils are predisposing factors. Sudden changes of body temperature are frequently followed by bronchitis, particularly if the surface of the body has been chilled after free perspiration. The mechanism of this reaction is probably the rapid extraction of heat by the cold air, especially moist cold air. The vessels of the mucous membrane undergo contraction followed by dilatation and free secretion of mucus. Under these conditions the remaining factor (bacteria) is furnished with a suitable culture medium. Bronchitis is therefore more frequently seen in changeable climates. Children are very susceptible because of their relatively large radiating surface, as also are aged people because of poor vasomotor tone, their circulation being incapable of accommodating itself to the sudden changes. That cold alone is insufficient to cause bronchitis was illustrated by an antarctic expedition the members of which were free from colds until after the opening of a bale of clothing which had been packed in civilization.

The rôle played by bacteria is now under investigation. That they are a causative factor under ordinary conditions may be doubted, but that a disturbed condition once established they are capable of perpetuating or intensifying it seems reasonable. While some investigators have found the finer bronchi free from organisms many others have demonstrated bacteria in both the bronchi and alveoli. That they are ordinarily present normally in the larger bronchi may not be doubted. From here, under proper conditions, they may readily invade the smaller bronchi. The protection against such invasion consists of the ciliated epithelium and the abundant bronchial secretion. These protecting factors may be inhibited in inflammatory conditions. The cases of bronchitis occurring in connection with the specific infections may be regarded as due to the causes that produce the infections. The organisms isolated from the sputum in the non-specific forms of bronchitis, however, are those which may be found under normal conditions. So many varieties may be present that to attribute the bronchitis to any one of them seems hardly justified. Pneumococci, streptococci, staphylococci, Friedlander's diplobacillus, Pfeiffer's bacillus, and numerous other bacteria, among them rarely the colon bacillus, have been reported as causes of bronchitis, but definite etiological proof is lacking. They may be regarded properly as only associated. In a series of respiratory complaints in children carefully investigated by Holt pure cultures were never seen. At times the influenza bacillus predominated, at other times the pneumococcus or the staphylococcus aureus; streptococci were present in fifty per cent. but rarely predominating, while the micrococcus catarrhalis was present in sixty-six per cent. and was regarded as

having no influence. There was no apparent relation between the symptoms and the bacteria, it being impossible to predict from the clinical findings what organisms would predominate. From a non-respiratory group of patients the same organisms were recovered. In twenty cases of bronchitis cultured at autopsy the pneumococcus was obtained in pure culture once, the *Bacillus influenzæ* twice and the *Staphylococcus aureus* six times. Lord found a single organism in thirty-three per cent. of 186 adult cases, but all subsequent cultures on the same cases showed mixed infections, thus casting doubt on any single organism as a cause.

Individual susceptibility must be taken into account, as among a group exposed to the same conditions only the susceptible will develop bronchitis.

Pathology.—Gross changes on postmortem examination may be very slight. The mucous membrane may show a coating of mucus or mucopus beneath which the surface may be congested and show small ecchymotic points. Other portions of the bronchi may be normal in appearance. The smaller bronchi may be plugged with exudate. On microscopical examination the epithelial lining may be found to be swollen or partially desquamated and the epithelial layers may show round cell infiltration. When the bronchitis has been more severe and the smaller tubes have been invaded these changes are all intensified, capillaries may be ruptured and the exudate at points hemorrhagic. The cellular infiltration is more intense and there may be some peribronchial reaction. In the severe bronchitis of children areas of collapse of alveoli are found, but areas of emphysema predominate. The bronchial lymph glands may be enlarged.

Symptoms.—The initial symptoms of acute bronchitis of the larger and medium-sized tubes and of the finer tubes are essentially the same. Following a coryza, pharyngitis, or laryngitis, or ushered in abruptly by chilly sensations, the attacks usually begin with slight fever, hoarseness, cough, and soreness and a sense of rawness beneath the sternum. The eyes may be injected from coughing and the muscles of the chest sore for the same reason. The cough at first is dry, frequent, distressing, and unproductive. Later it becomes less frequent and the expectoration becomes freer. The early expectoration is scanty and viscid, composed principally of mucus containing epithelial cells and occasionally streaked with blood. The later products of coughing are more easily expelled and are mucopurulent in character. The temperature is low in ordinary cases and soon declines, rarely persisting more than a few days. In cases involving the smaller tubes, however, the temperature may persist for two or three weeks. The cough also is more persistent and the soreness of the bronchi is more marked. There is almost always considerable mental depression. In children, because of the smallness and rigidity of the bronchi and the difficulty in expelling the secretion, the process frequently extends to the lobules and there is an associated bronchopneumonia. This is an essential element of so-called capillary bronchitis, more properly considered under the head of bronchopneumonia. At the beginning of the attack the bronchitis may be mild in character, but the development of a temperature of 103° to 104° associated with a decided increase in rate of respiration, slight cyanosis, restlessness, and the presence of areas of persistent fine râles should warn one that he is probably dealing with a bronchopneumonia and not with a bronchitis. In bronchitis the leucocytes are increased, being, in the mild cases from 10,000 to 15,000 and in the more severe, prolonged cases from 15,000 to 20,000. The percentage of polymorphonuclear cells varies from seventy-five to eighty-five.

Physical Signs.—These are almost entirely auscultatory. Palpation may show rhonchial fremitus. Auscultation reveals the characteristic large and small rhonchi associated with sibilant and sonorous râles and, in adults, with subcrepitant râles. All these râles may be made to change their character or to disappear on coughing. They differ in this respect from the persistent râles of bronchopneumonia. Breath sounds may be harsh and expiration prolonged.

Diagnosis.—The diagnosis in adults may be easily made, but it is impossible to say at first whether the affection is a primary bronchitis or is the initial exhibition of a case of pertussis, influenza, typhoid fever, tuberculosis, etc. If the blood examination shows a moderate leucocytosis with a relative lymphocytosis it would suggest pertussis. A Widal reaction and a leucopenia with a relative lymphocytosis and absence of eosinophile leucocytes would suggest typhoid fever. The demonstration of the bacillus of Pfeiffer in pure culture or strongly predominating would favor influenza.

A sputum examination and tuberculin reaction may aid in differentiating from tuberculosis, but it may be impossible to make a diagnosis during the first few days of an acute miliary tuberculosis with a fairly high temperature and negative sputum and signs similating a sever bronchitis. Cases giving localized persistent signs must be regarded with suspicion, particularly if the signs are at the apices. From pneumonia it may be differentiated by the history of a preexisting nasopharyngitis or laryngitis, by the absence of rapid respiration, by the moderate temperature, by the absence of a distinct chill, and by the physical signs. Enlarged bronchial glands may in children give symptoms which simulate bronchitis.

Prognosis.—In adults this is good for recovery but the proneness to recurrence must be borne in mind. In children, particularly the poorly nourished, and in institutional children, the prognosis must be guarded because of the frequency of the development of bronchopneumonia. Old people also tend to develop pneumonia in the course of bronchitis.

Treatment.—This consists of rest in bed, in a temperature of about 70° with plenty of fresh air. For the milder cases a laxative and hot drinks usually suffice. For the more severe cases, when the cough is dry and the sense of constriction marked, a mustard paste to the front of the chest three or four times a day gives relief. To aid in loosening the dry cough antimony is useful; one-thirty-second grain of tartar emetic and two grains of ammonium chloride in a teaspoonful of syrup of wild cherry may be given every hour for four doses, then every two hours.

In children a mustard paste in a strength of one part mustard to four or six of flour should be applied for about ten minutes every three or four hours. Difficulty in respiration may be relieved by producing vomiting by a teaspoonful of syrup of ipecac. If the cough is troublesome codeine may be given to adults in the form of a tablet of one-fourth or one-half grain as necessary. Children require no sedative for this stage. Inhalations of steam with tincture of benzoin give some relief. In the cases which run a course of two or three weeks with considerable expectoration the inhalations are most useful. A powder of codeine, gr. $\frac{1}{4}$ or $\frac{1}{2}$, and veronal gr. v., or trional gr. x., may be given to these patients to insure a night's rest. Digitalis in some form is useful to equalize the circulation in these prolonged cases. After the acute stage has passed the remaining cough is frequently greatly benefited by the exhibition of cod-liver oil. Vaccine treatment has shown no definite results.

Chronic Bronchitis.—The term chronic bronchitis must cover conditions arising from many causes and differing from each other in many particulars. All these conditions have in common chronic inflammatory changes in the mucous membrane and underlying structures of the bronchi.

Etiology.—Chronic bronchitis may be the result of repeated attacks of acute bronchitis; it may be due

to constitutional conditions, such as gout, nephritis, rickets, etc.; frequently, because the bronchial circulation involves both sides of the heart, it is associated with cardiac conditions that produce a chronic congestion of the lungs. Irritating atmospheric conditions and local lesions of the nasopharynx resulting in obstructing may be contributing causes. Asthma and emphysema are often associated and may have a causative influence. Arteriosclerosis and obesity are frequent precursors or concomitants of chronic bronchitis. Putrid bronchitis is associated with bronchiectasis, gangrene, or abscess of the lung. There are always associated bacteria for some of which at times a causative influence has been assumed. The most common organisms are those found also in acute bronchitis, but from the sputum of cases of putrid bronchitis have been isolated *Oidium albicans*, *Leptothrix pneumonalis*, *Bacillus coli communis*, and others.

Symptoms.—The cardinal symptom of chronic bronchitis is a persistent cough, usually with considerable purulent expectoration, especially in the morning. Sometimes, however, it results only in the expulsion of hard, pearl-like pellets after severe paroxysms. The cough varies in frequency and intensity and in the more severe cases is accompanied by asthmatic wheezing, dyspnea, and occasional cyanosis. Exacerbations occur which differ from ordinary acute bronchitis in their tendency to be more severe, to persist longer, and to be accompanied by asthmatic symptoms. In many cases there is loss of flesh and strength and later, when the heart partakes of the general malnutrition, cyanosis, and edema are added.

Pathology.—Changes are present in the larger bronchi, rarely in the smaller; the mucous membrane is gray and thickened from chronic edema or fibrous changes. The epithelium is altered and may consist of a single layer or of several irregular layers. In purulent bronchitis there is only a single layer. The walls of the bronchi are edematous, infiltrated with round cells, and show fibrous thickening; later they atrophy and are replaced by fibrous tissue. The cartilages atrophy and calcify and there is loss of muscular and elastic tone, and consequently emphysema develops.

Treatment.—During the exacerbations the treatment is that of acute bronchitis. Persons subject to chronic bronchitis should avoid exposure to sudden changes of temperature and if removal to a suitable climate during the winter months is impracticable should keep to the house in rough weather. Fresh air, sunshine, and rest are very important. The food should be simple with no excesses. Tobacco and alcohol must be very sparingly used. Exercise, walking, moderate golf, and driving or riding should be indulged in daily when weather permits.

For the cough inhalations give considerable satisfaction. They may consist of steam impregnated with compound tincture of benzoin or bicarbonate of sodium, or of an oil spray of menthol, eucalyptol, and iodine. For inhalation through a mask a mixture of equal parts of creosote, alcohol, and spirit of chloroform may be used.

When the cough is dry, ipecac, ammonium chloride, and alkalies are recommended. A teaspoonful of bicarbonate of sodium in a glass of hot milk on retiring frequently gives relief from the night cough. For the morning cough postural treatment is at times beneficial. The patient is accustomed to it by the gradual removal of the pillows and later by the gradual elevation of the foot of the bed. When a relaxed circulatory condition may be at fault digitalis is very helpful. For fetid bronchitis inhalations of carbolic acid, alcohol, and glycerin are useful and myrtol may be given internally in two to five minim doses, three times a day. Syrup of hydriodic acid and cod-liver oil may be taken between attacks. Much may be done in inhibiting the cough by personal effort assisted at times by a throat tablet. If a sedative is necessary codeine is to be preferred to morphine.

In recommending a climate one must be governed by the expectoration and the course. For the dry and moderate forms, abroad, Corsica, Madeira, Algiers, the Riviera, and the Italian Lakes, and in this country, southern California, the coast of Florida, the interior of North and South Carolina, Georgia, or Florida may be chosen. For the very moist varieties, Egypt, or in this country Montana, Wyoming, Colorado, New Mexico, and southern Arizona are suitable. The alkaline and sulphur springs have given satisfaction to some cases. Ems, Wiesbaden, Selters, Aix-la-Chapelle, Baden; Harrowgate in England; Richfield, Sharon, and the Sulphur Springs of Virginia in this country.

Breathing exercises which have for their object increased expiration with its improvement of the circulation in the right heart should be strongly insisted on.

Schilling (*Semaine Médicale* 1906, No. 38, p. 451) claims to have had prompt improvement after six to fifteen minutes exposure to the *x*-ray; the good effects lasting for two to three months.

The vaccine treatment of chronic bronchitis has yielded some good results in younger patients, but much cannot be expected from it when the changes in the bronchi are marked. Mixed autogenous organisms should be employed. To determine the specific organism complement fixation tests should be undertaken against those isolated. If these cannot be made the vaccine may be made from the mixed organisms isolated from the washed sputum. Vaccines should be tried where other methods have failed to give relief.

Fibrinous Bronchitis.—*Synonyms:* Plastic Bronchitis, Bronchial Croup, Bronchitis Crouposa, Bronchial Polypus. Although this is sometimes acute, it may in general be regarded as a form of chronic bronchitis characterized by recurring attacks of coughing during which casts of portions of the bronchial tree are expectorated. These attacks of coughing usually, but not necessarily, are accompanied by cyanosis and urgent dyspnea.

The disease has been recognized for centuries, the casts having been regarded as pulmonary vessels by Galen. The true fibrinous bronchitis must be differentiated from diseases in which pseudocasts may be expectorated, as pulmonary tuberculosis and diphtheria.

Posselt has divided the disease into two groups. In one of these the casts are composed almost exclusively of fibrin, are fairly firm in consistency with very few cells, and contain very little or no mucus. These casts are expectorated with only slight subjective disturbance. There is nothing about this group to suggest asthma. Of this type there are very few reported cases. There is no etiology. The attacks are seldom acute, the course being chronic or subacute.

The other group comprises the numerous cases which complicate asthmatic conditions. The casts are composed almost entirely of mucus with many cells. Crystals and eosinophile cells also occur. The course of cases in this group is more severe and more acute.

Etiology.—The cause is unknown. The distribution is that of chronic bronchitis. The individuals attacked are usually those whose resistance has been lowered by illness or by other causes. No definite exciting cause has been determined. The incidence is greater in males. It is uncommon under twelve years and over forty years of age, but no age is immune. The mucous form is often associated with asthma. Bacterial investigations have yielded no results as to the causative factor. Intercurrent skin diseases have been noted.

Pathology.—The casts as ordinarily seen are firm in consistency. Occasionally they may be streaked with blood. The size varies, the large ones measuring 10 cm. in length and showing branching to seven or eight degrees. Section of the larger portion shows them to be composed of an outer skin enclosing smaller whirls and cylinders and showing a flattened lumen. The smaller branches may be solid. They are composed usually in large part of mucin with a small amount of fibrin. The cell content varies; Posselt regarded the true casts as composed mostly of fibrin with very few cells. These composed of mucin are accompanied by many cells, mostly mononuclear. At autopsy the casts are usually found loose in the bronchi. The associated lesions are those of bronchitis. The organisms isolated have been the streptococci, staphylococci, and pneumococci. The structure of the casts suggests that their formation begins in the smaller bronchi and as they enlarge they protrude into the successively larger branches.

Fig. 1147.—Fibrinous Casts. Photographed by the late Dr. French from specimens obtained from a case coming under his own observation. (Three-fifths natural size.)

Fig. 1148.—Fibrinous Cast from Case Represented in Fig. 1147, showing nodular masses supposed to have come from the infundibula. (Three-fifths natural size.)

Symptoms.—The characteristic symptom is the expectoration of casts of the bronchial tree. This is preceded by a paroxysmal cough accompanied by a well-marked dyspnea and sometimes by cyanosis. The urgent symptoms are relieved by the expectoration of the cough and the patient's respirations may be normal between attacks. Sometimes, however, there are persistent slight dyspnea, cough, and elevation of temperature, all of which become exaggerated during the next attack. The individual paroxysms may be of short duration or may last an hour or more. The sputum is usually abundant, there having been "albuminous expectoration" in some cases. There may be moderate hemoptysis, but usually the casts are only slightly blood streaked. The casts vary in number and size.

The physical signs are not characteristic. Over an obstructed area the breath sounds may be absent or there may be a tympanitic or dull percussion note. Areas of tubular breathing or moist râles may be found. The intercostal spaces are sometimes retracted. Emphysema is of frequent occurrence.

There is loss of flesh and strength due to the recurring paroxysms and the accompanying bronchitis. The casts are the only characteristic symptom and for a satisfactory examination must be carefully teased out in water.

Prognosis.—This depends largely on the physical condition of the patient, the severity of the attack, the temperature, and the promptness with which the symptoms subside. Recovery is the rule, but relapses are common. Cases have terminated fatally during an attack but the usual cause of death is some intercurrent disease. Development of some degree of elevated temperature may indicate lung involvement. The prognosis must be guarded.

Treatment.—During the acute attack efforts may be made to help the expression of the casts. Emetics, particularly apomorphine, gr. $\frac{1}{10}$ by hypodermic injection, may be used to this end. Inhalations of steam may be useful. Potassium iodide has been used in full doses with success between attacks. Intratracheal injections of oil have been employed. Of very great importance between the attacks are attention to the general health and respiratory gymnastics along the lines laid down in the section on chronic bronchitis.

Joseph C. Roper.

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The literature to 1869 is covered by Lebert: Deutsches Archiv f. klin. Med., 1869.

The later literature has been reviewed by West: Practitioner, vol. xliii., 1889.

Bettman: American Journal Med. Science, vol. cxxiii., 1902, p. 304.

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Bronchopneumonia.—*Synonyms.*—Bronchial pneumonia, catarrhal pneumonia, lobular pneumonia, capillary bronchitis, etc. (The name bronchopneumonia is growing in favor, especially in this country, and is preferable.) There is always present bronchitis with areas of pneumonia. The latter are as a rule peribronchial, being confined to the immediate vicinity of the small bronchi, the bronchioles, and their atria, the cells adjacent to which are filled with exudate.

Etiology.—The disease is most common in the extremes of life, that is, in the aged and in children under five years old. Of the cases occurring in children, about one-third are primary, the others being secondary most often to the diseases of childhood. Of these, measles is the most frequently complicated by bronchopneumonia, and after this come pertussis, diphtheria, scarlet fever, influenza, and chickenpox. It will be noticed that these are diseases in which bronchitis is regularly present, or in which the upper air passages are involved in the morbid process. In older children and adults the disease may occur as a complication of any long-continued, severe illness, especially in those cases in which the mucous membrane of the mouth and pharynx becomes foul and the laryngeal reflexes are less effective than normally.

The predisposing causes in primary cases are old age or infancy, bad hygienic surroundings, the impure air of overcrowded, poorly ventilated rooms, bad feeding, and institutional life. We must also include among the predisposing causes the frequent presence of the diplococcus pneumoniæ and other pathogenic microorganisms in the healthy air passages.

The exciting causes are sometimes difficult to discover. Exposure to cold and wet is one cause, and this accounts for the greater frequency of the disease in the cold months. The predisposing causes of secondary bronchopneumonia are the same as those of the primary form of the disease, plus dorsal decubitus and the weakened condition due to the original disease. The exciting causes are again hard to determine. Exposure is one, but there is a something in addition which favors the growth and multiplication of the microorganisms usually present, even in health. In cases of deglutition-pneumonia the exciting cause is manifest.

The development of bronchopneumonia in old people is favored by the diminished powers of resistance and the less perfect expectoration.

Bacteriology.—In studying the flora of bronchopneumonia we have again to distinguish between primary and secondary cases. The microorganisms most commonly found are the diplococcus pneumoniæ, streptococcus, staphylococcus aureus and albus, Friedländer's bacillus, and Loeffler's bacillus.

In nearly all of the primary cases the diplococcus pneumoniæ is present, and in about half of these it exists alone. When not alone, it is most often associated with the streptococcus and much less frequently with the staphylococcus and the other organisms just mentioned. Infrequently the streptococcus is found alone.

In secondary cases it is the rule to find a mixed infection. The diplococcus pneumoniæ appears in about seventy-five per cent. of the cases, but seems less potent in giving character to the disease than the streptococcus. The diplococcus pneumoniæ, the streptococcus, the staphylococcus, and Friedländer's bacillus may each be present alone, unassociated with other bacteria, but in the case of Friedländer's bacillus, at least, this happens only rarely. The bacillus of influenza may also be present. Although,

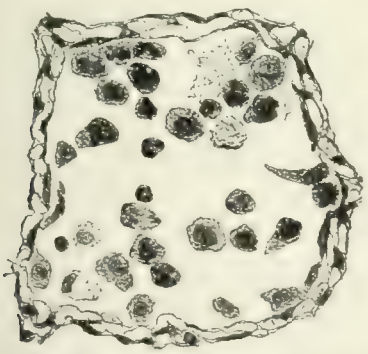

Fig. 1149.—Bronchopneumonia. Exudate in an air cell, consisting of exfoliated epithelium, a few pus cells, and a little fibrin. (From Delafield and Prudden.)

generally speaking, the streptococcus plays the most important part in bronchopneumonia complicating measles, it is precisely in this form that the diplococcus pneumoniæ is more often found in pure culture than in other secondary cases.

Holt reports six tuberculous cases which were studied by Wollstein, and in all of which the diplococcus pneumoniæ was also found; indeed, this organism gave the character to the disease in these cases, as clinically they were indistinguishable from those of an ordinary bronchopneumonia, the postmortem examination alone revealing their tuberculous nature.

Bronchopneumonia has in rare instances been found to be due to forms of streptothrix, and French investigators have reported the finding of the colon bacillus.

In deglutition-pneumonia the streptococcus and staphylococcus are most commonly found, and then, as a rule, in virulent form.

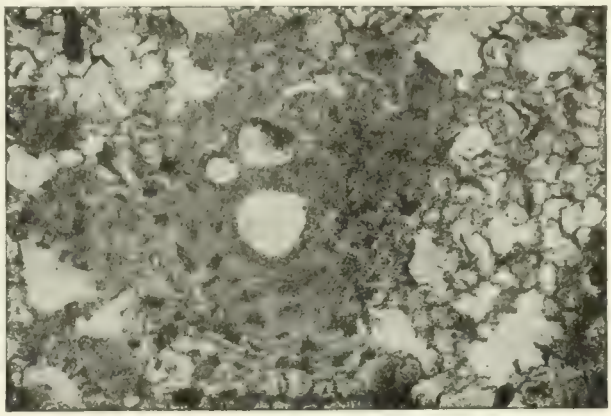

Fig. 1150.—Bronchopneumonia in a Child, Showing Single Lobular Pneumonic Area, with Bronchus in its Center. The thickened wall of the latter merges into the surrounding zone of pneumonia. Near the corners the accompanying emphysema is shown. (From Delafield and Prudden.)

Pathological Anatomy.—In about eighty per cent. of the cases coming to autopsy, lesions have been found in both lungs. These lesions consist essentially of those of bronchitis and of pneumonia.

When the chest is opened the pleural cavities are seen usually to contain little or no excess of fluid. The parietal and pulmonary pleural surfaces may be normal or the seat of a fibrinous pleurisy. The lesions of the latter consist of patches of fibrin which vary considerably both in extent and in character. At times they are almost invisible lusterless spots, and then again they may be quite large and thick (as much as half a centimeter thick) and more or less discolored. Such patches correspond closely to areas of superficial pulmonary consolidation.

The lungs do not collapse as completely as they normally should, though crepitation is found quite generally when the lungs are handled in the search for nodules of consolidation. The latter are most often found in the lower lobes posteriorly. There may be found collapsed areas, bluish or bluish-brown in color, set in a lighter background. These are areas of simple atelectasis, and will yield to gentle inflation through a tube inserted in a bronchus. The bronchial nodes are invariably congested and enlarged. The heart—the right side more commonly—may be dilated.

On section, the pneumonic areas stand out a little, are of a dark mahogany color, or more or less marbled with gray, smooth or finely granular, and moderately wet; only a small amount of dark blood escapes from the vessels. Such areas vary greatly in size, and may be close together or widely separated. Near the center of each a bronchus is seen, white or gray, because of the exudate which it contains. The unconsolidated lung tissue may be normal, but more often it is congested and edematous, particularly behind. An emphysema, usually vesicular, is often present, being most pronounced anteriorly. Upon

section of the areas of atelectasis, dark fluid blood escapes; the cut surface is seen to be smooth, with occasional lobules projecting above it. Creamy pus can be pressed from the smallest bronchi; portions carefully removed are found to contain no air and they sink in water.

With the aid of the microscope we see that the exudate within the bronchi of the consolidated areas is composed of leucocytes, mucus, desquamated epithelium in various stages of disintegration, a few red blood cells, and the microorganisms responsible for the condition. The walls of the bronchioles and bronchi are swollen and infiltrated with new small round cells with more or less indistinct contours and having large nuclei. (See Plate XLIX.)

Northrup mentions a mechanical dilatation of the smaller bronchi. These dilatations, which are for the most part fusiform in shape, are found with especial frequency in the lower lobes. They are associated, according to this authority, with three conditions: (1) Weakened bronchial walls; (2) abundant secretion within the bronchi; and (3) impermeable tissue surrounding them. The dilatation is due to the secretion being forced by each inspiratory impulse from larger to smaller bronchi. The process, which is observed in children between three and five years of age, occurs more often after the fifth day of the disease. The dilatations disappear entirely on the recovery of the patient.

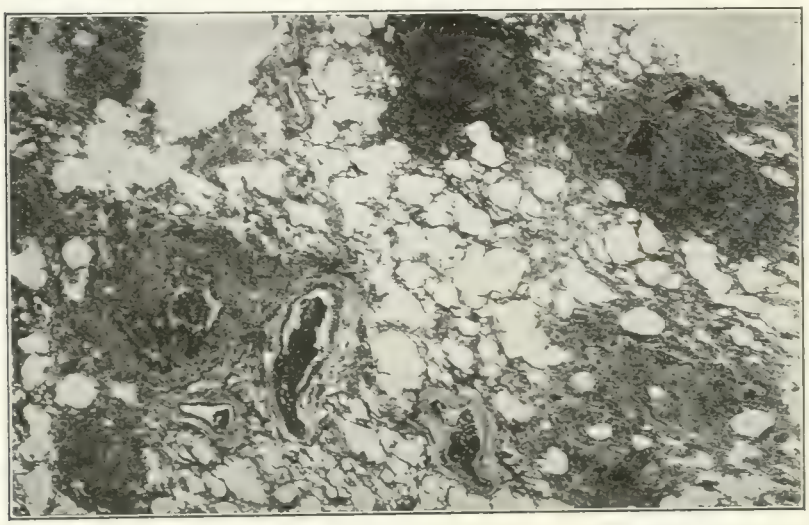

Fig. 1151.—Bronchopneumonia in an Adult, Showing Several Areas of Consolidation, with the Central Bronchus Filled with Exudate. Marked emphysema may also be seen in parts of the section. (From Delafield and Prudden.)

As the walls of the bronchioles are swollen and infiltrated with new cells, so also are those of the atria and of the air sacs, including the partitions between the air cells. The capillaries are engorged with blood and small hemorrhages may be noted here and there. The air cells, air sacs, and atria are filled with leucocytes, swollen desquamated epithelium, occasionally a few red blood cells, and sometimes also a little fibrin.

In deglutition- or aspiration-bronchopneumonia the process is more intense, the infiltration with leucocytes often resulting in suppuration and gangrene.

In the areas of atelectasis the bronchi are seen to be filled with pus and swollen and detached epithelia, and the walls of the bronchioles are infiltrated; the air cells and sacs are partially collapsed, the diminished lumen being filled with swollen and proliferating epithelia and pus cells. The blood-vessels are tortuous and gorged with blood. Here and there are hepatized lobules. In some cases the emphysema is very marked (see Fig. 3828).

The bronchial lymph nodes may or may not show a cellular infiltration. They are always congested.

Symptoms.—The symptoms may be most obscure, even misleading, making it almost impossible, for a period of several days, to reach a correct diagnosis.

Prodromal Symptoms.—In primary cases, as in acute bronchitis, the early signs are a general malaise with more or less anorexia, slight elevation of temperature, acceleration of pulse and respiration, and cough, dry or with mucous expectoration in patients old enough to perform that important act. The invasion may resemble that of lobar pneumonia, being marked by a chill or convulsion and by rapid rise of temperature to 103° or 104° F. or over; or the invasion may present no characteristic features, the symptoms resembling those of typhoid fever or meningitis. In the cerebral cases there may be repeated convulsions, apathy, photophobia, retraction of the head with rigidity of the neck, and an absence of physical signs of consolidation.

In *secondary* cases, the prodromal symptoms and the invasion are masked by the symptoms of the primary disease. The invasion is gradual, seldom marked by a chill or convulsion, the child becomes restless, the temperature rises, and the pulse-respiration ratio diminishes. If there was a cough before, it becomes worse, or one develops if there was none previously. If there is any expectoration it is mucopurulent in character. An early symptom may be the cough—painful, frequent, and hacking—and it often continues after resolution has taken place.

The temperature varies according to the extent of the lesions, the virulence of the infection, and the general condition of the patient; apparently also it is influenced by the variety of microorganism present. It may rise slowly or very suddenly, as a rule to 103° or 104° F., and it averages moderately high, with sharp elevations, most often in the afternoon, but at times in the early morning. The variations in the temperature curve gradually become less and less; in favorable cases the general trend is downward, restoration to the normal being by lysis. In unfavorable cases the trend of the curve is constantly upward, the temperature sometimes going as high as 107° F. The temperature may be of a high, continued type, this usually portending a fatal issue. On the other hand, in greatly debilitated subjects the temperature may rise little if at all above 100° F. The usual termination of such cases also is death.

Pain is not a constant symptom, and as a rule it occasions little trouble.

Cyanosis is quite common, but there is little or no dyspnea. When it is caused by atelectasis the temperature remains unaffected or falls a little. The skin is often cold and clammy. These symptoms disappear upon the removal of the cause of the atelectasis, and the patient is then about as well as before the attack. If the cyanosis persists for more than a day or two, however, the result is a fatal one.

In well-marked cases, the respiratory rhythm is changed. Instead of the inspiratory murmur being nearly continuous with the expiratory, the pause which in health was after expiration and before inspiration, is now transferred and is after inspiration and before expiration. The child quickly draws its breath, holds it, then with an explosive grunting sound expires and without pause inspires. The expiration is prolonged and loud. There may be Cheyne-Stokes respiration.

Gastroenteric symptoms, such as loose green stools without vomiting, are frequent in infancy. The urine may become scanty, high colored, and with a trace of albumin, but casts are rare.

In cases ending in recovery amelioration of all symptoms may occur at any time from the fourth day to the third or fourth week. In mild cases it is looked for from the fourth to the eighth day.

Resolution takes from seven to fourteen days in avorable cases. Relapses are common.

Physical Signs.—It may be that for days no signs at all can be discovered within the chest, and it frequently happens that no signs of consolidation are found at any time during the course of the disease. In primary cases the first signs are due to congestion and bronchitis; they are either localized in one or more areas, or are generally distributed. The results of percussion may be negative, or there may be slight dulness. On auscultation we detect feeble breathing, which later has a higher pitch over the affected areas, and is associated with fine sibilant and coarse sonorous râles of the same or of wider distribution. These râles may disappear when the patient coughs. A little later, very fine moist râles are heard, as a rule, only over one or more areas, usually in the lower lobes behind. The vocal fremitus is unaltered. In such cases the pneumonic areas are deeply seated, small, and scattered.

The signs of consolidation, when present, vary according to the degree of consolidation, the area involved, and its proximity to the chest wall. In well-marked cases percussion reveals the existence of dulness in varying degree, associated at times with a sense of resistance. The vocal fremitus is increased only over areas of fairly complete consolidation. Auscultation reveals the presence of the râles above mentioned, only they are more marked and apparently closer to the examining ear; the breathing is bronchovesicular or diminished; the voice sounds approach the bronchial in character. In the cases in which there is a considerable area of complete consolidation, the signs more nearly approach those of lobar pneumonia, a disease which occurs in young children more often than was formerly believed. The dulness and vocal fremitus, however, are less than one would expect to find with voice and breathing of such a bronchial character. The signs of bronchitis are rarely general, and are most numerous in and near the edges of the consolidated areas. Friction sounds are infrequently present, usually only in cases of complete consolidation extending to the pleura.

It may be necessary to make the patient cough in order to develop the sounds of bronchitis, or crying may bring out, in an area of diminished voice and breathing, a marked bronchial quality. In extreme cases the breathing becomes shallow and very rapid, eighty or more to the minute, with retraction of the xiphoid and ribs and playing of the alæ nasi. The right ventricle of the heart may be found increased in size.

When resolution begins the signs of consolidation, which were the last to come, are the first to go. They may disappear very rapidly or they may persist for days or weeks. The signs of bronchitis subside less rapidly, often being found as late as from two to four weeks after resolution has begun. The blood count, as a rule, reveals a leucocytosis of from 12,000 to 20,000, of which from sixty-five to eighty-five per cent are polymorphonuclears. The significance of these counts is not fully understood, but considered with other signs and symptoms they help in determining the severity of the infections, the resistance of the body, and the prognosis.

Complications.—We rarely find any pleurisy, except when there is marked pulmonary consolidation that reaches to the pleura. The simple fibrinous pleurisy is the most common.

The possibility of empyema must always be borne in mind. Abscess of the lung complicating bronchopneumonia is found in about seven per cent. of the cases that come to autopsy; these abscesses are usually minute and multiple, and not clinically discoverable. Gangrene is less frequent. Tuberculosis may complicate any bronchopneumonia, and in fatal cases cannot be diagnosed before death.

As in lobar pneumonia, so in bronchopneumonia, a purulent meningitis may occur, and may mask the symptoms of the primary disease.

Pericarditis is found at times, almost always in cases in which there is marked consolidation in the left lung. The rarity of endocarditis makes it hardly worth mentioning.

It is common to find functional derangement of the gastrointestinal tract, as shown by vomiting and diarrhea, which are serious, not in themselves, but in that they reduce the patient's chances of recovery in the other fight.

Nephritis is not a common complication, and when it does occur it is usually of an acute exudative type and does not much affect the course of the original disease.

Diagnosis.—The diagnosis of primary bronchopneumonia from lobar pneumonia is at times very difficult. It must be made on the age, history, and mode of invasion, on the character of the temperature, on the sputum (when there is any), and on the physical signs; the latter alone furnish positive evidence.

The diagnosis from pleurisy with effusion or from empyema must be settled by an exploratory puncture, several dry taps with a large-caliber needle being necessary to establish the absence of fluid.

As an aid to diagnosis in uncertain cases, in children two years of age or under, Northrup gives the three following points:

1. The pulse-respiration ratio tends to depart from the normal, which is as four is to one, and approximates or exceeds three to one. For instance, instead of being 80 to 20, it approximates the ratio of 120 to 40.

2. Fever; persistent elevated temperature, whether remittent, intermittent, or uniform.

3. Râles; subcrepitant and crepitant over a circumscribed area or areas, and especially if these râles are found on one side only.

Malaria is excluded by the absence of malarial organisms, by normal spleen, and by no history of exposure in malarious regions; the presence of leucocytosis also argues against malaria.

Treatment.—Much can be done to prevent the development of the disease and to help the patient pass safely through it, when once it is established.

I would outline the treatment under the following heads: (1) Prophylaxis. (2) General management of the disease. (3) Diet and feeding. (4) Special treatment: (*a*) by drugs; (*b*) by serum therapy. (5) Symptomatic treatment: (*a*) to relieve pain; (*b*) to lower the temperature and moderate the nervous symptoms; (*c*) to stimulate the heart, in order to prevent cardiac failure or to overcome it if present; (*d*) to stimulate respiration.

Prophylactic treatment is very important. Care must be taken to see that children are sufficiently clothed yet not overclothed; that they are much out

of doors, and that while indoors they are in well-ventilated rooms, with a temperature not over 68° or 70° F. during the day and ten or more degrees lower at night. Children ill with any diseases, particularly those that are most likely to be complicated by bronchopneumonia, should be turned often in bed, now on one side, then on the other, now on the back and then on the abdomen. Bronchitis in an infant should be most carefully treated, as such cases, especially if neglected, are very prone to develop bronchopneumonia. In all cases the mouth should be carefully washed at least once daily, preferably with some alkaline antiseptic solution; and antiseptic nasal sprays are advisable as preventive measures.

General Treatment.—Infants are better for being much held in the nurse's arms; older patients are to be put to bed at once and the bowels moved by calomel, in doses of one-fourth of a grain every half hour for six doses, or until the desired effect is obtained. The sick-room should be large, light, and well-aired; there should be a steady renewal of the supply of fresh air. In cases with much consolidation or toxemia or both, the window or windows should, as in lobar pneumonia, be open all of the time, excepting a short while before and during the times when the patient must be uncovered. The patient must not feel cold. In winter a warm hood is worn and a hot water bag may be needed at the feet. When the bronchitis appears to be the predominant lesion, hot moist air with vapor of creosote is used. This may be obtained by the use of a tent and croup kettle or by running steam into the room. In the Babies' Hospital, New York, the steam room is used as routine treatment.

It is well to establish a more or less strict isolation, and to disinfect the patient's rooms and their contents before they are used by another person. Especially should this be done in secondary cases.

Diet.—Great care should be exercised in the management of the diet, as the turning of the tide one way or the other often depends upon it. Plenty of cool water, not iced, should be at hand, and the patient should be encouraged to drink it.

Special Treatment.—Drugs can often be given to advantage by inhalation. The child should be placed under a tent and some kind of a vaporizer employed. A variety of drugs may be added to the water or it may be used by itself. The addition of creosote gives particularly good results. Turpentine, compound tincture of benzoin, and terebene may also do good service when exhibited in this way. The inhalations should be given for from eight to fifteen minutes at a time, every two to six hours. The cough is often greatly relieved by such inhalations. The administration of drugs which, it is believed, can make the blood a less favorable medium for bacterial life, is always to be considered. For this hexamathylenamine with twice as much benzoate of sodium is at present our best combination for this purpose. This should be given in aqueous solution every two hours. The only harm that may result is painful urination, and this fact may be used as a guide as to dosage. A child of a year may be started on hexamethylenamine, gr. 1 (0.065) ten times a day.

Serum or Bacterin Therapy.—We must trust the future to give us some serum or bacterin which singly or together will raise the body resistance to such a point that the toxins will be neutralized and the growth of the invading organisms stopped. No certainly good results from such treatment are yet reported. My experience leads me to believe that the early use of mixed bacterins (pneumococcus, staphylococcus, and streptococcus) prevents the involvement of new areas, but has little or no effect on the consolidation already present.

Symptomatic Treatment.—The application of hot mustard poultices (one to five) every four to six hours makes the patient feel better and should be used. In feeble patients with embarrassed respiration heavy poultices must be avoided. In these cases, capsicum in vaseline, "mustard leaves" or camphorated oil fortified with turpentine give a good counterirritation. Pain severe enough to demand the administration of some form of opium is unusual. When such a condition does exist, small doses of Dover's powder are quite efficient.

Ordinary temperatures, say those under 104° F. rectal, do not in themselves call for special treatment. However, it may be advisable, when this degree of temperature is reached, in order to control the nervous symptoms, such as sleeplessness, restlessness, or delirium, to reduce the temperature. There is no doubt that this is best done by tepid rubbing. The patient, a child, is put in a tub of water at 100° F. (38.5° C.), and well rubbed with bare hands. Usually eight to twelve minutes is a suitable length for the bath. This gives nervous equilibrium as well as lower temperature, and no undesirable after-affects. Coal-tar products are to be avoided.

Both cardiac and respiratory stimulants may be needed. Of the first class we will mention alcohol in the form of brandy or whiskey, strychnine, and caffeine. None of these is to be administered as a routine treatment. As a matter of fact, however, very many, indeed nearly all, patients with secondary bronchopneumonia need cardiac stimulation, the chief indication for such being a weak, rapid, irregular pulse. The physician should determine how much alcohol it is desirable to give in the twenty-four hours and have it administered in small divided doses, well diluted with at least from six to eight times its bulk of water. A child one year old may need only half an ounce of brandy during the day, or he may need as much as two ounces. The dose, whatever it is, should be reduced as soon as possible, and the alcohol should not be continued for too long a time. Strychnine is not to be given so frequently as alcohol. To a child of the age mentioned gr. $\frac{1}{100}$ to gr. $\frac{1}{50}$ of strychnine may be given every three or four hours. Caffeine is of great service and where needed may be given hypodermatically as caffeine-sodiobenzoate, gr. ½ (0.032) every three hours, to a child of six months. It is often best to use two of these drugs, giving them alternately.

The seat of the disease being in the lungs, it is very natural that respiratory stimulants should be called for. Strychnine helps here just as it does in cases of cardiac failure, and in addition to it we can use atropine, caffeine, and oxygen, all of which may be necessary in cases of respiratory failure. We should not wait until the patient is *in extremis* before giving oxygen; when administered it should be considerably diluted with air. Infants in collapse are greatly benefited by one or two injections of gr. $\frac{1}{1000}$ (0.00006) of atropine and a mustard bath.

In emergencies, adrenalin ♏ j of $\frac{1}{10000}$ strength for every year of age may be given hourly for twenty-four or less doses.

In adults venesection is of great service in orthopnea with lividity.

After an attack of bronchopneumonia general tonics are indicated, and it is especially advisable for the patient to have a change of air, preferably to a warm, dry climate, where he should remain for several weeks.

Prognosis.—This must always be guarded, for bronchopneumonia is a dangerous disease. The mortality of all cases, considered together, is between sixty and seventy per cent.

The mortality of primary cases varies greatly, viz., from ten to fifty per cent., depending upon the previous condition of the patient upon the virulence of the infection, and upon whether the child is an inmate of an institution or not. In private practice the maximum mortality is about thirty per cent.

In secondary institutional cases the mortality of infants under one year of age is appalling. In certain diseases it reaches and stays at 100 per cent. for months at a time.

The prognosis depends upon the child's age, surroundings, and previous condition, and upon the nature of the infection. Rachitic children developing bronchopneumonia are almost sure to succumb. Bronchopneumonia is most fatal when associated with pertussis, next with measles, and then with diphtheria. This order, however, is a matter about which statistics differ.

Holt says the shortest cases are the most fatal; that the only termination under ninety-six hours is a fatal one, and he says further that, in cases of over two weeks' duration, the prognosis grows worse with each day of continued temperature.

Patients having a low temperature, little or not at all above 100° F., are usually in a condition of low vitality, and consequently about seventy-five per cent. of them die. The mortality of cases in which the temperature reaches 106° F. or over is about eighty-five per cent. The most favorable prognosis is in cases with a fairly even temperature curve, one that does not run to either extreme, and does not vary much one way or the other from 103° or 104° F., during the period of activity of the infection.

A steeple chart with great rises and correspondingly great drops of temperature, simulating a pus temperature, usually indicates a mixed or a streptococcus infection, and the prognosis is worse than in the cases with a more even curve.

A convulsion or two at the onset of bronchopneumonia does not affect the prognosis unfavorably, but when convulsions come later in the course of the disease they do affect it, and that decidedly for the worse.

Bronchopneumonia may terminate in resolution, suppuration, gangrene, chronic bronchopneumonia, or death. HENRY E. HALE.

Bronchoscopy and Direct Laryngoscopy.—*Definition.*—Bronchoscopy is a procedure using tubes which serve as specula by drawing out of the way tissues which normally obstruct the view, or by dragging the tissues to be examined into a new position in the line of direct vision. All bronchial specula, or bronchoscopes, as they are called, are straight and rigid instruments. They are usually introduced through the mouth, which procedure is called "upper bronchoscopy," but they may be introduced through a tracheotomic wound when the procedure is called "lower bronchoscopy." These terms are unfortunate as they are apt to be confused with bronchoscopy of the upper and lower lobe bronchi, known as upper lobe bronchoscopy and lower lobe bronchoscopy respectively. Better terms are "oral bronchoscopy" and "tracheotomic bronchoscopy." In tracheotomic bronchoscopy the bronchoscope is simply inserted into the trachea through the wound. Oral bronchoscopy, on the other hand, requires a very important preliminary procedure known as direct laryngoscopy, which consists in exposing the glottis to direct inspection by a straight and rigid instrument known as a laryngeal speculum. This procedure is called direct laryngoscopy in contradistinction to indirect laryngoscopy, the old and well-known procedure by which the interior of the larynx is inspected, not directly, but indirectly by its image reflected in a small mirror placed in the pharynx.

History.—In 1894, A. Kirstein of Berlin devised a method of direct laryngoscopy which he called "autoscopy." In 1897 he described tracheoscopy by inspection through the glottis exposed to view by his method of autoscopy. In 1897 Gustav Killian demonstrated the feasibility of passing straight and rigid tubes through the glottis into the tracheobronchial tree by reason of the great elasticity of this tree; and he demonstrated that these tubes could be used for inspection when illuminated by the headlamp of Kirstein. In the same year Killian removed a foreign body from a bronchus of a living child and thus demonstrated the usefulness of the procedure. The safe removal of foreign bodies from the bronchi by laryngologists in various parts of the world soon established bronchoscopy as an operation of low mortality, useful for the removal of foreign bodies from the trachea and bronchi. The search for foreign bodies, in cases where they were or were not present, led to the discovery of lesions undemonstrable in the living by any other method. This discovery and the consequent direct application of medicaments have now firmly established bronchoscopy as a procedure available for the diagnosis and treatment of diseases of the lower air-passages. Direct laryngoscopy independently of its usefulness as a stage in bronchoscopy has come to be recognized as the method of choice for operations upon the larynx. Many laryngologists in various parts of the world have contributed to the further development of the instruments and the technique for direct laryngoscopy and bronchoscopy. Bronchoscopic study has yielded important data on the physiology and living anatomy of the tracheobronchial tree.

Usefulness.—For general diagnostic purposes in the adult the old mirror method of indirect laryngoscopy remains as useful to-day as ever, and in defects of laryngeal motility it is far superior to the newer direct method because the presence of the laryngeal speculum excites reflex spastic movements. But to get a view of the larynx by the indirect method requires cooperation of the patient, hence in children mirror examination is practically impossible. By the direct method the larynx of any child can be easily and promptly examined in a few seconds without any anesthetic, general or local, provided the operator has acquired the knack. The great importance of this procedure may be realized from the statistics of the author's clinic which shows that out of 100 cases of laryngeal diseases in children eighty-seven per cent. had been given diphtheritic antitoxin before admission at some stage of their disease, under a mistaken diagnosis of laryngeal diphtheria because of inability of the profession in those days to examine the larynx in children. In adults, as well as in children, laryngeal operations of all kinds, such as removal of benign laryngeal growths, galvanopuncture of tuberculous infiltrations, the removal of foreign bodies—in fact all manipulations in the interior of the larynx, are carried on with the greatest precision because the work is guided by direct instead of indirect vision whereby all anteroposterior motions are apparently reversed by the mirror. In cases of malignant growths a specimen can be removed with the utmost precision so as to include a portion of the normal as well as of the neoplastic tissue, thus enabling the pathologist to give a dependable report. Having aided thus in making a diagnosis of malignancy the usefulness of direct laryngoscopy ends; for as yet, the cases that justify any operation whatever (early intrinsic malignancy of very limited extent) are so successfully dealt with by thyrotomy with mucoperichondrial dissection that endolaryngeal operation is rarely, if ever, justifiable. Direct laryngoscopy is in general use for the introduction of tubes in the Elsberg and other methods of intratracheal insufflation anesthesia. The field of bronchoscopic therapeutics is steadily enlarging. Pyogenic infections have been treated locally and also by autogenous vaccines obtained from material removed bronchoscopically and uncontaminated by secretions of the mouth or pharynx. In certain types of asthma relative cures have been reported from local treatment of endobronchial conditions. Obstinate cough has been cured by endobronchial

local applications of argyrol to non-specific local ulcerations. Benign growths have been removed. Luetic and tuberculous lesions have been diagnosticated. Bronchoscopy for foreign bodies has yielded most brilliant results, considering the recency of its discovery and development. Out of 108 cases of bronchoscopy for foreign bodies in the author's clinic, the foreign body has been removed in 103. Of the five failures, three were before the full development of the present instrumentarium and technique. Two relatively recent cases were absolute failures because the foreign body could not be found. In both of these the foreign body had entered so small a bronchus that the invaded branch could not be located. The larger bronchi are few and easily searched, but the small bronchi are exceedingly numerous, and the search of all blindly is unwise.

Mortality and Dangers.—Even approximate accuracy as to mortality is almost impossible. Work in the interior of the air passages differs from all others in that fatal dyspnea may suddenly appear at any time and unless the operator is familiar with the problems from long experience the patient may die from lack of prompt aid. Such deaths have occurred in the class of cases with which bronchoscopy has to deal, and such a death may be due not to the bronchoscopy but to the lack of promptness in performing it. Therefore, the only reliable statistics are those of the large clinics and the skilled operators. These statistics show that direct laryngoscopy is practically without any mortality when performed on a healthy subject. The same may be said of bronchoscopy. The dangers arise chiefly from general anesthesia, cocaine poisoning, inexperience, faulty technique, stenosis due to a foreign body, or to disease. Skilful operators have had a mortality of about three per cent. from all causes, which is exceedingly low considering the very high mortality of these cases if unaided by bronchoscopy. Occasionally in infants subglottic edema will result from the use of too large a bronchoscope or from trauma in introduction. This accident, an exceedingly rare one in skilled hands, is promptly relieved by tracheotomy, which

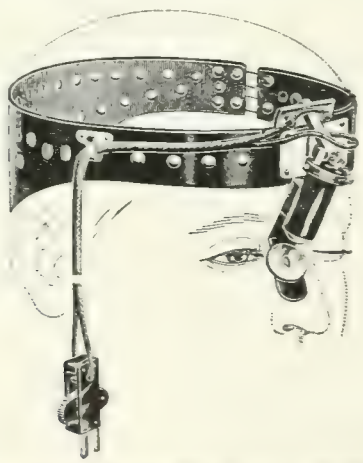

Fig. 1152.—Kirstein Headlamp for Direct Laryngoscopy.

under these circumstances is an operation of very low mortality. Aneurysm, very hard arteries, thymic tracheostenosis, and similar conditions introduce an element of danger in bronchoscopy, and aneurysm is a contraindication except for the removal of foreign bodies.

Instruments.—All bronchoscopes of practical use have been straight and rigid tubes. The chief differences in the various forms have been in the method of illumination. Killian in his early work used the Kirstein headlamp (Fig. 1152) and he still uses it for direct laryngoscopy and direct laryngeal operating. W. Brünings[1] uses a hand lamp attached to the proximal end of the laryngeal speculum and the bronchoscopes slide through the laryngeal tube, the distance of extension being regulated by a watch spring (Fig. 1153). Otto Kahler[2] uses a different form of proximal lamp. In all forms of proximal lamps the light is projected down the tube from the proximal end. The author, like Ingals[3] and the majority of American laryngologists, prefers the distal form of illumination shown in Fig. 1154, B, in which a very

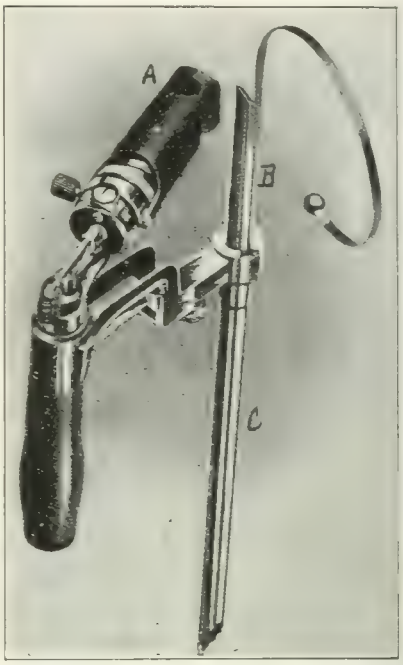

Fig. 1153.—Brünings' Bronchoscope. The illuminating apparatus, *A*, is shown swung to the left to permit of the insertion of the inner tube, *B*, into the laryngeal tube, *C*.

small lamp is carried down to the distal end of the instrument on a light carrier. Inasmuch as good work has been done with all forms of illumination, it is probable that successful work depends more upon the skill and especially upon the amount of practice of the operator and the training of his assistants, than upon the form of illumination. Various accessory instruments are needed, a few of which are shown. For the removal of particular foreign bodies many special instruments have been devised, such as pin cutters, safety-pin closers, mechanical spoons for friable bodies, etc. Doubtless many more will need to be devised. Each case is a problem in itself, the problem being not so much the removal of the foreign body, which could be done by main strength, but to remove the instruder without endangering the life of the patient, wherein lies the great value of bronchoscopy for foreign bodies. The following is a list of tubes and accessories necessary for direct laryngoscopy and bronchoscopy:

1 child's slide speculum.
1 adult's slide speculum.
1 adult's bronchoscope 9 mm.×40 cm.
1 child's (7 to 16 years) bronchoscope 7 mm. × 40 cm.
1 child's (1½ to 7 years) bronchoscope 5 mm.×30 cm.
1 infant's (up to 1 year) bronchoscope 4 mm.×30 cm.
6 sponge holders.
2 forceps, plain jaws, 30 cm., and 45 cm.
1 thimble bite block.
1 double bronchoscopic battery and 2 cords.
12 extra lamps.

Radiographic Aid in Bronchoscopy for Foreign Bodies.—In foreign body cases fluoroscopic examination is very misleading. A radiograph should be taken in every case of suspected foreign body even though the suspected intruder is not dense to the ray because the foreign body is not always what it is supposed to be, and furthermore lesions are often revealed by the ray indicating the location of a foreign body which, itself, does not show. A dark lung indicates that the corresponding main bronchus is occluded. The occlusion of the upper, lower, or middle lobe bronchi will cause the corresponding lobe to cast a shadow if occlusion is nearly complete. Twice in the author's experience a radiograph revealed a lung abscess due to a peanut kernel, though the kernel itself did not show. Foreign bodies when located by a bath, a laxative, and a liquid breakfast at least five hours before the bronchoscopy. The mouth should be thoroughly cleansed with a tooth brush, and rinsed with thirty-per-cent. alcohol.

Asepsis.—When it is considered that we encounter diphtheria, pneumonia, syphilis, tuberculosis, pyogenic cocci, and various other infections, the presence of which may not be known to us even after we are through with the patient, it behooves the conscientious surgeon to be as scrupulous in his aseptic technique as if he were opening the brain or abdomen. He must not permit laxity on the part of his operating room organization, a thing prone to happen because the field cannot be sterilized. It must be remembered that the patient is more or less immune to the organisms he himself harbors; yet infections introduced

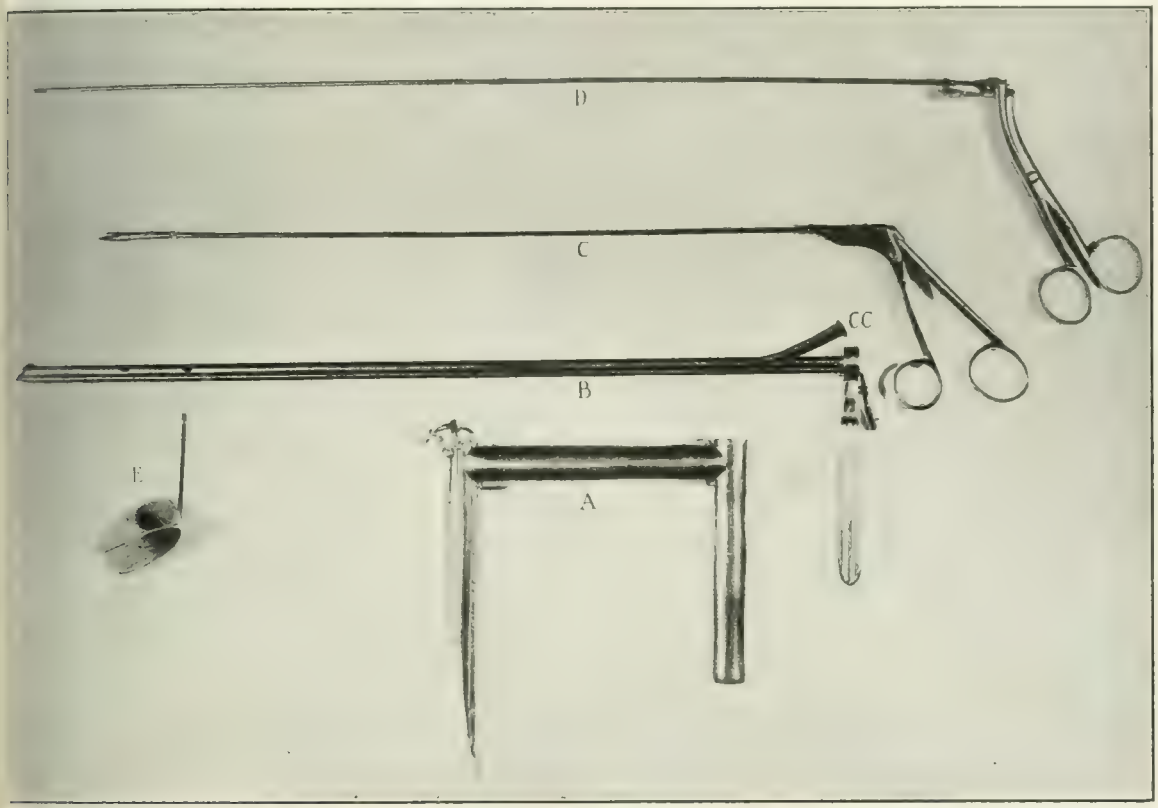

Fig. 1154.—Author's Instruments for Direct Laryngoscopy and Bronchoscopy. *A*, Laryngeal speculum; *B*, bronchoscope; tube for insufflation of anesthetic shown at *CC*.; *C*, laryngeal biting forceps; *D*, bronchoscopic forceps; *E*, bite block. The tube is for insufflation of ether during esophagoscopy, gastroscopy, or direct laryngoscopy. The tube, *CC*, is used instead in bronchoscopy.

n the larger bronchi are easy to find with the bronchoscope; but a relatively small intruder which falls nto the lowest and smallest bronchus it can enter, lmost at the periphery of the lung, is often very lifficult to find not only because of the smallness f the bronchial branch, but because of the great umber of such branches. Therefore, the most ccurate radiographic localization becomes of the reatest aid. For this purpose the four greatest ids are: A lateral radiograph, triangulation from adiographic exposures in different positions, the oyce calipers (Fig. 1155), and the author's system of uperimposing a proper sized negative of the tracheo-ronchial tree (Fig. 1156) over the negative of the pa-ient showing the foreign body.

Preparation of the Patient.—When time permits, he patient should be prepared as for any operation, from other sources, even though nominally the same, may be extremely virulent to him. One thing is absolutely essential, namely, that everything be prepared and in readiness, including all possible needs, before work is commenced; for moments are precious and unpreparedness may mean death. Particularly useful is an oxygen tank cleansed and prepared aseptically with sterile tubing, and wrapped with sterile towels.

Anesthesia.—Direct laryngoscopy and bronchoscopy when skilfully done are practically painless. The only need then for any anesthesia is for the lessening or abolition of reflexes, chiefly those of vomiturition and coughing, and for the prevention of apprehension which intensifies the reflexes. A general anesthetic lessens somewhat the difficulties encountered by the unskilled in the introduction of

instruments, but its use for this purpose is unjustifiable. For direct laryngoscopy in children no anesthetic, general or local, is ever required. Cocaine is exceedingly dangerous in children and its use is needless. In all dyspneic cases in either adults or children a general anesthetic is exceedingly dangerous and should never be given. In direct laryngeal operations for conditions such as papillomata in the intruder, which is then likely to drop into the deeper air passages, that it is better in most instances to use no anesthetic whatever. If it is desired to use one, cocaine should be sprayed in during inhalation rather than applied with a swab as hereinafter mentioned. When, however, the direct laryngoscopy is only preliminary to the passage of a bronchoscope adults will require thorough cocainization of the

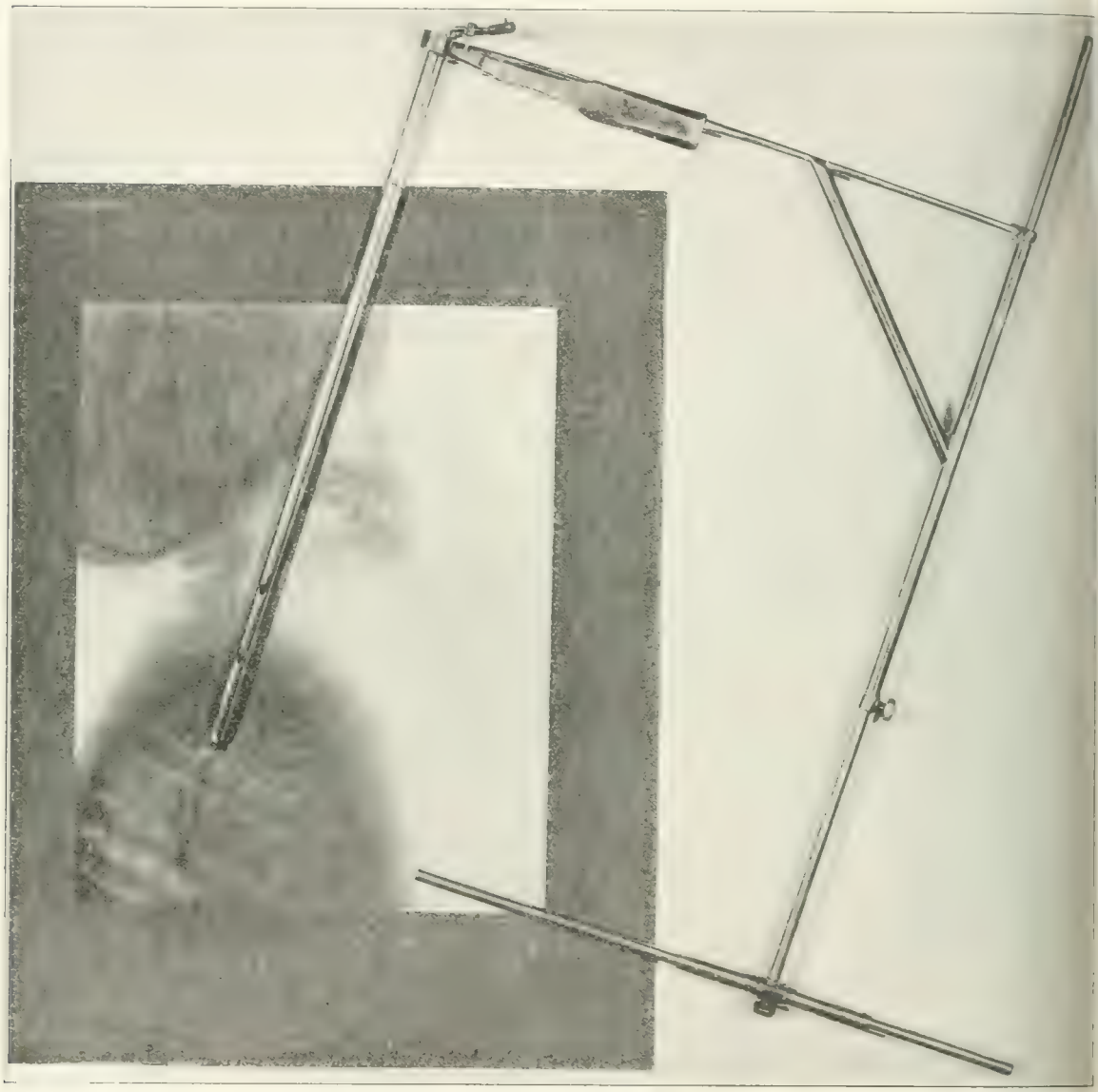

Fig. 1155. Calipers for the Localization of a Bronchially Lodged Foreign Body. The distance of the foreign body from the skin surface is thus registered from the lateral radiograph. The calipers are then detached, later reattached after the bronchoscope is introduced. The position of the foreign body in the lateral plane is marked on the skin from the anteroposterior radiograph without calipers, by the anatomical landmarks.

children, no anesthetic, general or local, is needed; because these growths are quite insensitive and the reflexes of children need not interfere with work. In adults, however, the reflexes will require cocaine locally, for operations on the larynx, and also in some instances when only a diagnosis is to be made. Any attempt at cocainization of the larynx in a case of laryngeally lodged foreign body is so apt to dislodge mucosa of the larynx and especially of the epiglottis in diagnostic cases. In difficult foreign-body cases general anesthesia is used by most operators for both children and adults. In the author's clinic, no anesthetic, general or local, is used for bronchoscopy in children except in very complicated removals of foreign bodies, and not even then if the child is in the slightest degree dyspneic. In cases of long and sharp

foreign bodies, such as pins and needles, it is often wise to get the full relaxation of deep ether anesthesia to prevent coughing lest the point be forced to perforate. Large doses of bromides (gm. 4 for an adult) if there is time for their action, materially assist in lessening the cough and other reflexes. Atropine hypodermically as advocated by Fletcher Ingals lessens secretion, which is a great aid. The best procedure in local anesthesia is to give a preliminary swabbing

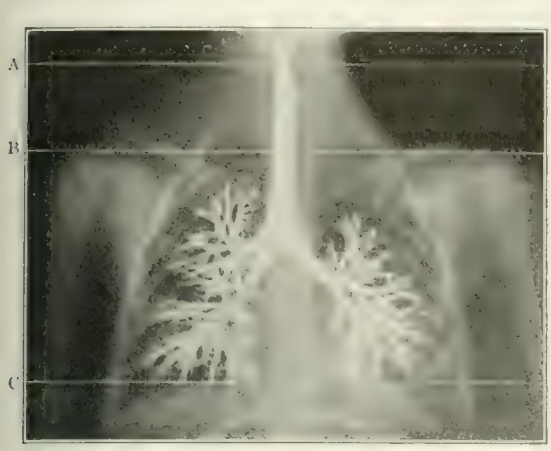

Fig. 1156.—Negative of the Tracheobronchial Tree Used in Different Sizes for Localization of a Foreign Body Preparatory to Bronchoscopy. This negative is superimposed upon the radiographic negative of the patient. *A*, Level of the vocal cords; *B*, level of pleural dome; *C*, level of dome of diaphragm. These visceral landmarks are used instead of the bones, whose position relative to the viscera varies widely.

of the laryngopharynx with a cotton swab held in a Sajous' laryngeal forceps and saturated, but not dripping, with an eight-per-cent. cocaine solution. The epiglottis is exposed with the speculum and is painted with a gauze sponge held in a straight sponge holder, and saturated, but not dripping, with a twenty-per-cent. cocaine solution. The posterior surface of the epiglottis especially must have a careful painting. Then the same solution is applied in the same way to the upper laryngeal orifice. Next the subglottic trachea is painted. After the introduction of the bronchoscope, the trachea is painted, giving especial attention to the region of the bifurcation, to the posterior tracheal wall and to the particular bronchus which is to be entered first. In all these applications it is necessary to remember that cocaine is an exceedingly dangerous drug requiring caution in its use. Of course most of the solution is thrown away in the swabs. A prolonged contact of the swab is much more efficient than a mere painting of the mucosa. This is important to remember when severe cough is excited every time a foreign body is touched; though a skilful operator will work along in spite of severe coughing, which indeed often ceases after a while. After the beginning of the cocainization at the epiglottis every moment is precious, so that work should be as rapid as is consistent with orderly, careful procedure. When general anesthesia is used it should be ether started in the ordinary way with the mask. After the patient is anesthetized and the bronchoscope is inserted, the ether is insufflated through the anesthetizing attachment suggested by Dr. T. Drysdale Buchanan, timing the insufflations to coincide with the patient's inspirations. Should ether fail to give as complete relaxation as is deemed necessary, chloroform may be insufflated with comparative safety after the full stimulant effects of the ether are evident.

Technique.—The most important part of the introduction of the bronchoscope is the proper exposure of the glottis, and the most important part of adequate glottic exposure is the position of the head and neck of the patient. The patient may be sitting or recumbent, but in either case the position of his head and neck is relatively the same. This position consists in an anterior placing of the head and neck, with the cervical spine straight, not curved, and with extension of the head at the occipito-atloid joint. The correct position is shown in Fig. 1157. The patient sits upon a low stool, and the first assistant sits behind the patient on a stool of ordinary height and holds the patient far forward toward the operator. The tendency of the patient is to throw his head and neck backward, thus curving his cervical spine backward and rendering exposure of the larynx almost impossible. The operator sits on a stool of ordinary height and should not stand lest he fall into the error of trying to pry open the passages by using the upper teeth as a fulcrum, which will also render glottic exposure difficult. The battery cord being connected and the light glowing, the operator with the index of his right hand raises the upper lip of the patient to keep it out of the way, while with his left hand he introduces the laryngeal speculum until the epiglottis comes into view. (If local anesthesia is to be used, note the instructions under that heading.) The spatular end of the speculum is passed posteriorly to the epiglottis and down over it for about one centimeter in a child, two centimeters in an adult. If the epiglottis slip away, deeper insertion is needed; but a very common error is too

Fig. 1157.—Showing the Position of the Patient, Operator, and Assistants for Laryngeal Operation by the Direct Method under Local Anesthesia.

deep an insertion, the operator mistaking one or the other aryepiglottic fold for the epiglottis and consequently inserting the extremity of the speculum into one or the other of the pyriform sinuses. If this occur, withdrawal to the dorsum of the tongue and a fresh start is advisable. The error is best avoided by careful identification of the epiglottis, careful following of the middle line down over the dorsum of the tongue, and careful work on the part of

the assistant to keep the patient's head exactly plumb and square and facing the operator without any twist or inclination to either side. Having mastered the epiglottis the motion imparted to the speculum is a pulling downward and toward the operator, as if the operator were trying to pull the epiglottis and hyoid bone out through the neck with the *tip* of the distal end of the speculum. This displaces the bulky musculature of the base of the tongue and the tissues attached to the hyoid bone forward out of the line of sight and exposes the glottis; so that the observer may look down into the trachea if the glottis be open, for the trachea is now in line with the axis of the speculum and with the visual axis of the observer, as shown schematically in Fig. 1158. Should there be any difficulty in exposure of the anterior commissure the index-finger of the assistant who holds

FIG. 1158.—Schema Showing the Position of the Speculum in Direct Laryngoscopy.

the head, by making counter-pressure on the thyroid cartilage externally in the neck, will bring the anterior commissure backward into view. The laryngeal operation may now be proceeded with, using biting, cutting, or crushing forceps, or the galvanocautery, as the case may require. In case of foreign body in the larynx, removal should never under any circumstances be attempted with the patient in the sitting position, because if the intruder should be dislodged and escape, as is very apt to happen, it will almost certainly fall into the lower air passages. Removal of laryngeally lodged foreign bodies should be attempted only with the patient in the Trendelenburg position so as to gain the aid instead of the antagonism of gravity. If bronchoscopy in the sitting position is the object, the bronchoscope having its own cord and light is inserted and the observer's eye is transferred to the bronchoscope. The lip of the bronchoscope is turned to correspond with the long axis of the glottic chink, that is, the handle is placed horizontally. At the next inspiratory opening of the glottis the bronchoscope is gently pushed through until a few centimeters of the distal end lies within the trachea. The heavy speculum is now removed leaving the light and delicate bronchoscope in position to be gently guided and moved about by the hand of the observer. To prevent the tube being bitten, the bite block is kept between the teeth by the assistant. No gag should be used, or, at least, wide gagging must be carefully avoided, because it forces the thick lingual mass along with the inferior maxilla down onto the hyoid bone so firmly that anterior displacement of this mass by the speculum becomes difficult or even impossible. Bronchoscopy is rarely done in the sitting posture except in adults and for diagnosis only, using local anesthesia or none at all. Children require the recumbent position for better control if no anesthetic is used; and for safety if any anesthetic is used. In all foreign body cases the recumbent position is imperative in order that gravity shall not assist inspiration in drawing the intruder deeper, should the intruder be free to move. The procedure is relatively the same in the recumbent posture except a slight difference in the handling of the instruments. It is imperative that the patient's head shall not hang over the end of the table in the Roser position, which position is erroneously advised in many textbooks. It must extend beyond the table so as to be free to move, but it must not hang. It must be supported high up with extension only at the occipito-atloid joint. This is the Boyce position and is thus described by Dr. John W Boyce:[4]

"In all this work safety demands that the mouth, pharynx, and esophagus (or trachea as the case may be) be brought into a straight line, not by a crowbar like action of the tube, but by holding the head steadily in extreme extension with the mouth widely open. Not only does lateral pressure add to the operator's difficulty, but it also entirely prevents any sense of what the point of the tube is touching. Trial with an unanesthetized patient will show that if the head is simply allowed to hang over the edge of the table, not only is an unnecessary strain thrown upon the ligaments of the neck, but full extension is not as well secured as by proper support of the head. For this reason it is best to detail a second assistant to hold the head and hold the bite block, impressing him with the importance of the matter and his entire responsibility therein. To carry him out of the operator's way it is necessary that he shall hold the head at arm's length and to hold it in this position steadily for fifteen or twenty minutes a support is necessary. The weight of the head is so little that the matter seems easy, but if the assistant's arms are unsupported, about the time the most critical point of the examination or operation is reached his muscles will be trembling. Nor is it possible to rest him by any shift of position after the tube is started. After many unsuccessful trials, it has been found that the best position is as shown in Fig. 1159. The patient is drawn forward until the tops of his shoulders clear the table by from four to six inches, and the bite block is inserted on the left side. The assistant is placed on the right side of the patient's head on a stool of appropriate height, as though on a side saddle; his right leg beneath him in the kneeling position, his left foot supported on a stool twenty-six inches lower than the top of the table; his right forearm is passed beneath the patient's neck, supporting it; his right index holds the bite block drawing it strongly backward. His left hand rests on the left knee, grasps the head strongly at or in front of the bregma, bending it backward and exerting a certain degree of upward pressure. The exact proportion of backward and upward pressure cannot be described, but is readily appreciated on trial, especially if the assistant has actually experienced the difference in sensation when the head hangs free and when it is properly supported in extreme extension."

The introduction of the bronchoscope through the mouth in the recumbent position is shown schematically in Fig. 1160. The different relations of the parts renders practice in this position necessary as well as practice in the sitting position, experience in the one not aiding much in the other. As in the upright position, in order to obtain adequate glottic exposure, the upper teeth must not be used as a fulcrum and the head must be raised by the suspension of the weight of the patient's head more or less on the *tip* of the spatula, though support and extension on the occipito-atloid joint are maintained as described by Dr. Boyce. The epiglottis is identified, the spatular end of the speculum is passed posteriorly to the epiglottis and the epiglottis is raised, that is dragged anteriorly, anatomically speaking, and the glottis exposed. If any difficulty in exposure of the anterior commissure is encountered, counter-pressure by the assistant's index-finger on the thyroid cartilage externally, as before mentioned, will obviate the difficulty. When only direct laryngoscopy is con-

templated, the larynx may be inspected with very much greater comfort to the patient by slight flexion of the head, that is, anteriorly on the chest, the head resting on a pillow as in ordinary recumbency in bed, the operator standing at the left side of the patient. This was first demonstrated by Dr. R. H. Johnston.[5]

This position is excellent for laryngeal examinations and endolaryngeal operations. It is not so well adapted to bronchoscopy, though if preferred the bronchoscope may be introduced through the glottis in this way, and then the head can be brought into the Boyce position. In this procedure, extreme care must be used that no trauma is done to the larynx and especially to the subglottic tissues. Returning to the consideration of bronchoscopy in the recumbent position, the bronchoscope is inserted through the speculum, the handle extending horizontally to the right so as to bring the lip of the slanted

Fig. 1159.—Position of the Patient and Assistant for Oral Bronchoscopy.

end of the bronchoscope in the proper position for easiest insertion through the glottis. The patient often at this moment holds his breath and may have some laryngeal spasm. It is better to wait for an inspiration with which the glottis will open, and the bronchoscope is then quickly inserted. If the patient is not anesthetized and will cooperate, he may be told to take a deep inspiration. If profoundly anesthetized, no halting of the ryhthmic respiratory excursions is noticed and the bronchoscope is readily introduced into the trachea.

The inexperienced will often find that the bronchoscope has gone into the esophagus. In a case with great dyspnea this may be fatal not only by default in not entering the trachea, but also directly by the compression due to the bulk of the tube in the esophagus plus the bulk of the foreign body in the trachea. The error can be detected by failure to receive the expiratory tracheal blast, though there is a slight esophageal respiratory movement, and by the pink smooth collapsing esophageal walls instead of the ringed open tracheal tube. Having introduced the bronchoscope into the trachea, the first step is to observe whether the axis of the trachea and that of the tube coincide and if they do not, they should be made to coincide at once so that no resistance is felt and no danger of trauma from the tube mouth is

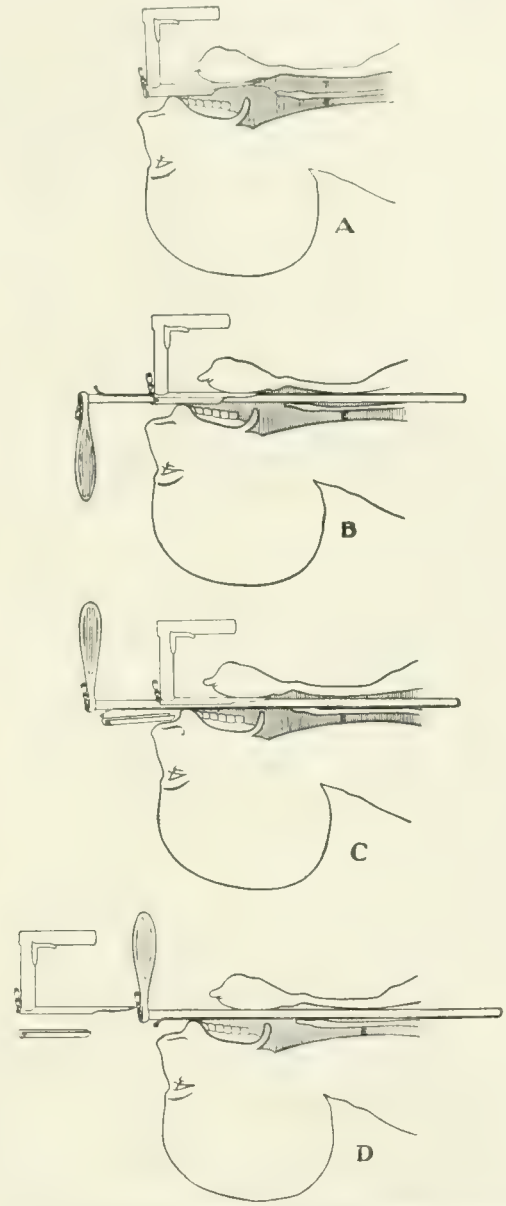

Fig. 1160.—Oral Bronchoscopy. Schema illustrating the passing of the bronchoscope into the recumbent patient. *A*, Laryngeal speculum in position exposing the glottis; *B*, bronchoscope passed through the speculum into the trachea; *C*, slide of speculum removed; *D*, speculum removed leaving bronchoscope in the trachea unencumbered by the heavy speculum.

incurred. The bite block being in place, the slide speculum is removed as shown at *D*, Fig. 1160. Passing downward the first landmark is the carina or spur between the right and left bronchus. If this is not noticed it is because the right bronchus is practically the continuation of the trachea, the left bronchus resembling a lateral branch to such an extent that

the carina is overlooked at the left of the tube mouth and is passed. Should this occur, the bronchoscope is rotated so that the handle is horizontal and to the left. This brings the lip of the bronchoscope against the left tracheal wall, and if in addition the patient's head is moved to the right the bronchoscope will enter the left bronchial orifice and the carina will be seen. This use of the lip of the bronchoscope, together with the opposite position of the head, is useful in the entering of any desired branch bronchus; and especially the upper lobe branches which are the most difficult of any of the larger bronchi to enter. Secretions, which are in some instances troublesome, are best removed by swabs made of small folded gauze sponges held in the sponge holder. These sponges should be as large as will readily pass through the tube. If there is much secretion the sponge is pushed down beyond the distal end of the bronchoscope. The resulting reflex cough will force the secretion into the tube mouth when the secretion will be withdrawn by the withdrawal of the sponge, just as a pump lifts out the water that is above the plunger. This is more rapid and efficient for bronchoscopic purposes than any form of aspirator. Further procedure depends upon the purpose for which the bronchoscopy is done. The identification of lesions, the removal of specimens of tissue, or of secretions for investigation or autogenous vaccine therapy, or the removal of foreign bodies—all these procedures are under guidance of the eye, and education of the eye and the fingers is absolutely essential to safe and successful work. The trained eye will in every case see the forceps close with certainty upon the object and upon nothing else. CHEVALIER JACKSON.

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Broom.—See *Scoparius*.

Brouardel, Paul Camille Hippolyte.—Born in Saint-Quentin, France, February 13, 1837. He received the degree of Doctor of Medicine in 1865. In 1879 he was chosen Professor of Medical Jurisprudence, and in 1881 Dean of the Faculty of Medicine of Paris. He died in August 1906. He made numerous contributions to medical literature, and of this number the following deserve special mention: "Le secret médical," second edition, 1893; "Cours de médecine légale de la Faculté de Médecine de Paris," seven volumes; "La pendaison, la strangulation, la suffocation et la submersion," 1896; "L'Infanticide," 1897; and "Traité de médecine et de thérapeutique" (in association with A. Gilbert), ten volumes. (Pagel.) A. H. B.

Broussais, François Joseph Victor.—Born December 17, 1772 at St. Malo in Brittany. He served for a number of years as surgeon in the French Navy and later was appointed surgeon in chief of the military hospital at Val de Grace. In 1831 he was appointed Professor of General Pathology at the Faculté de Médecine of Paris and held this chair to the time of his death on November 17, 1838. He was the founder of the theory of disease, called Broussaisism, which was allied to, though in its therapeutic development the opposite of the Brunonian system. In studying the lesion of typhoid fever he noted the frequent occurrence of hyperemia, inflammatory manifestations, ulceration, etc., in the intestine, and this led him to look for, and naturally to find, signs of "irritation" in other diseases. From this he formulated the theory that all acute disease is due to irritation or "irradiation" proceeding from inflammation of the gastroenteric tract. He believed that all vital processes are the result of stimulation; the sum total of the stimulation in the body is, however, a fixed quantity, and therefore an excess of stimulation in one part necessarily results in a diminution elsewhere, this disturbance of the equilibrium of "irritation" being the essence of disease. The treatment of disease therefore should consist in efforts to reduce the excess of irritation in the gastroenteric tract by means of diet, cataplasms, and depressant remedies.

FIG. 1161.—François Joseph Victor Broussais.

Broussais's principal works, written before the development of "broussaisism," were: "Histoire des phlegmasies ou inflammations chroniques," 1808: "Examen de la doctrine médicale généralement adoptée," 1816; and "Examen des doctrines médicales et des systèmes de nosologie," 1821.

T. L. S.

Brown, John.—Born in Buncle, Scotland, in 1735. In youth he manifested talents of an exceptional character and it was thought that a great future lay before him, but his manners were so offensive and his habits so ill-regulated that even his best friends were in time unable to tolerate him. Having taken up his abode at Edinburgh, in or about 1760, he pursued the study of medicine with assiduity for several consecutive years. The celebrated Cullen befriended him at first and put him in the way of earning a living, but before long the friendship between the two was broken up, and eventually Brown became one of Cullen's bitterest enemies. In 1779 he published a book (under the title of "Elementa medicinæ") which gave him considerable celebrity. After having been thrown into prison for non-payment of his debts, he became more and more dissipated, indulged very freely in the use of laudanum, and finally died of cerebral apoplexy in 1788, at the comparatively early age of fifty-three.

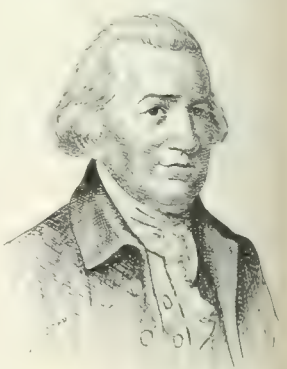

FIG. 1162.—John Brown.

It is difficult to understand, at the present day, how Brown's "Elements of Medicine" should have created such a stir in the medical world as it appears to have done. Even German and French physicians took an active part in discussing the peculiar theories put forward in this book. (See *Brunonianism*.)

A. H. B.

Browne, Sir Thomas.—Born at London, England, in 1605. He studied medicine at the University of Leyden, Holland, and received his doctor's degree from that institution. After his return to England, in 1634, he settled in Norwich. In 1665 he was elected an honorary member of the College of Physicians, London. Charles II, in passing through Norwich in 1671, bestowed on him the honor of knighthood. He died on October 19, 1682. His skull is preserved in the museum of the Norwich hospital.

Sir Thomas Browne owes his celebrity almost entirely to the fact that he wrote and published two books which excited very great interest, not only in Great Britain and on the Continent of Europe, but also, in later years, throughout the British Colonies. These books are entitled, respectively: "Religio Medici," and "Pseudodoxia Epidemica; Enquiries into very many commonly received Tenets and commonly presumed Truths." The first authorized edition of the *Religio Medici* was published in 1643; The *Pseudodoxia* was issued in 1646. The *Encyclopedia Britannica* says that the "*Religio Medici* was a puzzle to his contemporaries, and it is still hard to reconcile its contradictions. . . . . It is the confession of a mind keen and sceptical in some aspects, and credulous in others. . . . . The *Pseudodoxia Epidemica*, written in a more direct and simple style than is usual with Browne, is a wonderful storehouse of out-of-the-way facts and scraps of erudition, exhibiting a singular mixture of credulity and shrewdness. Sir Thomas evidently takes delight in discussing the wildest fables." A. H. B.

Brownian Movement.—The phenomenon known as Brunonian or Brownian movement or motion, so called after Robert Brown, a Scotch botanist, who first described it in the *Edinburgh Philosophical Journal* in 1828, consists in extremely rapid vibratory movements of microscopic particles suspended in fluids. It occurs in simple suspensions of solid particles in water or other fluid as well as in colloidal solutions. Up to a certain point the activity of the movements is increased by concentration of the suspension and also by the smallness of the suspended particles. It is apparently not an electrical phenomenon, nor is it influenced by light. It is physical, not vital, in nature, and may be due, as has been suggested, to the fact that the solid particles are in unstable equilibrium and so are influenced by and render visible the molecular movements of the fluid in which they are suspended. T. L. S.

Brown-Séquard, Charles Edward.—Born in Port Louis, on the island of Mauritius, Indian Ocean, April 8, 1817. His father, Edward Brown, came from Philadelphia, Pa., while his mother, Séquard by name, was a native of France. In 1838 he visited Paris for the purpose of completing his medical studies, and received from the university of that city, in 1840, the degree of Doctor of Medicine. From that time onward he devoted himself to experimental investigations in regard to the composition of the blood, animal heat, the spinal cord and its diseases, and the muscular, nervous, and ganglionic systems; and, as a result of this experimental work, he felt warranted in undertaking the treatment of diseases of the nervous system. From time to time during the following score or more of years he made a practice of visiting London and some of the larger cities in the United States for periods varying from a few weeks or months to several years. On such occasions he delivered a certain number of lectures on topics related to his specialty and also carried on a good deal of consultation practice. In 1860 he was appointed physician to the Hospital for the Paralyzed and Epileptic. In 1864 he was appointed professor of pathology at Harvard University. In 1869 he resigned his professorship and returned to Paris. In 1873 he again came to the United States and practised medicine for a few years in New York. In 1878 he was elected to the Chair of Experimental Medicine in the Collège de France, as the successor to Claude Bernard. He died in Paris, April 2, 1894. (Pagel.)

Fig. 1163.—Charles Edward Brown-Séquard.

The majority of Brown-Séquard's published writings relate to nerve-physiology, and pathology, and in this department of medicine it may justly be claimed that he has made valuable additions to our stock of knowledge. In 1858 he founded the "Journal de la physiologie de l'homme et des animaux," and continued its regular publication up to 1863 (six volumes). In 1868, in association with Charcot and Vulpian, he established the *Archives de physiologie normale et pathologique*. A few years before his death he acquired considerable notoriety through his advocacy of the use of testicular juice for the relief of senile debility. A. H. B.

Brownsville, Texas, a town of 6,130 inhabitants, is situated on the north bank of the Rio Grande River, opposite Matamoras, in the extreme southeastern corner of the State. It is a port of entry, and has a warm, moist climate. It is not a health resort, and is mentioned here simply to indicate the climatic conditions which exist in this section of the country.

Climate of Brownsville, Texas, Latitude, 25° 53′; Longitude, 97° 26′. Period of Observation, Seven and One-Half Years. Elevation of Place of Observation Above Sea Level, Twenty-Eight Feet.

Data.	January.	July.	Year.
Temperature (Fahrenheit scale)—			
Average mean	59.5°	84.4°	73.1°
Average range	17.2°	15.2°	.....
Mean of warmest	66.9°	92°	.....
Mean of coldest	49.7°	76.8°	.....
Highest or maximum	83°	98°	.....
Lowest or minimum	18°	68°	.....
Humidity—			
Average relative (per cent.)	79.6	71.9	76.3
Precipitation—			
Average in inches	2.10	2.63	32.03
Wind—			
Prevailing direction	N.	S. E.	S. E.
Average hourly velocity in miles.	7	6.9	6.9
Weather—			
Average number clear days	8.1	13.3	116.3
Average number fair days	8.1	14.2	148.9
Average number fair and clear days.	16.2	27.5	265.2

Note.—If the above chart is not self-explanatory to the reader, he is referred to the article upon *Baltimore*, where in a similar table some of the terms are commented upon.

Edward O. Otis.

Brown's Wells.—Copiah County, Mississippi.

Post-office.—Brown's Wells. Hotel and cottages.

Access.—Via Illinois Central Railroad to Hazelhurst, thence five miles by automobile to Springs.

Brown's Wells are situated near the central part

of Mississippi, 40 miles south of Jackson and 150 miles northeast of New Orleans. The roads are excellent, and there is automobile service for every train. The location is among the pine hills of Mississippi, though hickory, oak, and other growths abound. The climate here is very salubrious, and extremes of either heat or cold are seldom observed. The temperature rarely falls lower than 20° F. in the winter or rises above 98° F. in the summer. The elevation above the sea level is 600 feet. There are no flies and no mosquitos. The resort is open for the reception of visitors all the year. Seven springs are found in the neighborhood. The analyses of these several springs are given in the following table.

Mineral constituents.	Well No. 1.	Well No. 2.	Well No. 3.	Well No. 4.	Well No. 5.	Well No. 6.	Well No. 7.
Sodium nitrate	0.018	0.0387	..		. .	0.0462	0.0089
Lithium chloride	Trace.	Trace.	.	Trace.	0.0500	Trace.	Trace.
Magnesium chloride	... ..	.....	.	....	1.6921	1.205	0.0834
Sodium chloride .	3.971	4.131	6.2381	4.3725	5.4661	1.500	5.3770
Sodium sulphate	3.417	3.8275	6.7678	3.4569	2.9134	.... .	... ...
Potassium sulphate..	1.288	2.0935	9.0365	2.1472	1.9872	1.982	1.3335
Aluminum sulphate .	.....	.....	3.8478	10.5747	2.3228	.. ..	.. ....
Magnesium sulphate .	33.67	35.10	20.5799	26.6180	.....	4.191	41.605
Calcium sulphate..	8.484	9.3975	27.5176	42.9846	25.5686	1.6375	10.555
Iron sulphate .	. ...	.....	9.4446	1.0614	.....	... .	... .
Calcium phosphate	Trace.	Trace.	.....	Trace.	.....	Trace.	Trace.
Magnesium carbonate	.....	.....	....	.....	12.9098	..	.....
Calcium carbonate.	.....	.....	7.2875	4.8972	1.8721	. .	....
Calcium bicarbonate	30.91	27.405	.....	.....	.....	16.265	37.400
Sodium bicarbonate .	0.269	0.1469	.	.....	.....	0.1959	0.147
Manganese bicarbonate.	1.961	3.773	.	.....	....	0.4035	1.921
Iron bicarbonate ..	8.945	4.9815	0.1798	5.7129	4.1161	0.0776	23.285
Aluminum oxide .	0.614	0.0987	.....	.....	.....	. .	0.5598
Silica	4.793	4.257	1.3409	1.2490	....	2.3325	2.898
Organic matter .	.....	.....	0.6413	0.4860	0.5000	. .. ..	. .....
Arsenic acid	. .....	.....	.. .	Trace.	.....	. .. ..	.. ..
Total grains per gallon. . .	98.322	95.2116	98.8818	103.5604	59.3982	29.7900	124.1647

The analyses of Wells Nos. 1, 2, 6 and 7 are given upon the authority of A. M. Muckenfuss, Ph. D., Director of the Chemical Laboratory, University of Mississippi. Analyses of Wells No. 3, 4 and 5 are given upon the authority of Prof. A. L. Metz, Professor of Chemistry, Medical Department of the Tulane University of Louisiana.

The waters of Wells Nos. 1 and 2 are alkaline in reaction. These waters are indicated in conditions of gastric acidity, nervous dyspepsia, neurasthenia, and malaria. The water of Well No. 3 has an acid reaction and acts as a tonic to the relaxed mucous membrane of the stomach and intestines, being of service in cases of chronic diarrhea and dysentery. Wells Nos. 1 and 4 are the original wells upon which the reputation of the resort was established. These waters are used in liver and kidney affections, enlarged prostate, rheumatism, and gouty affections.

Wells Nos. 5 and 6 contain many of the chemical elements of the other wells but in a less concentrated form. Thus they are especially suited to the use of children and others who find the more active waters too strong. Well No. 7 contains more of the purgative elements than do the other wells.

From the above description it can be seen that, although grouped comparatively near together, a singular variety seems to characterize the waters of these wells, in relation to both chemical constitution and therapeutic action. EMMA E. WALKER.

Brown-tail Moth.—The caterpillar of this moth, *Euproctis chrysorrhea*, is covered with poisonous hairs which may enter the skin and cause much irritation and even in some cases painful suppurating ulcers. See *Insects, poisonous.* A. S. P.

Bruecke, Ernst Wilhelm.—Born in Berlin, Prussia, on June 6, 1819. He studied at Berlin and Heidelberg and received the degree of Doctor of Medicine in 1842. In 1844 he was made a "Privatdozent" in physiology in the University of Berlin. In 1849 he was elected to the regular chair of physiology and advanced microscopic anatomy in the University of Vienna, Austria. He performed regularly the duties of this chair up to the year 1890, when, in accordance with the law of the university, he was obliged to retire, with the title of Emeritus Professor. His death occurred from influenza on January 7, 1892.

As evidence of the esteem in which Bruecke was held by the university authorities and by his colleagues in Vienna it may be stated that, during his professorship he received the following special honors: he was made a regular member of the recently founded Vienna Academy of Sciences; the title of Hofrat was conferred upon him; he was made a life member of the Austrian House of Lords (1879); he was chosen Rector of the University, etc. In his published writings Bruecke did not—as is the habit of most of the modern physiologists—treat of one or two questions in which he took a special interest, but reported the results of investigations which he had made in widely different departments of physiology. The following selected list of a few of his publications confirms the truth of the statement just made: "Gründzüge der Physiologie and Systematik der Sprachlaute für Linguisten und Taubstummenlehrer," Vienna, 2d edition, 1876; "Neue Methode der phonetischen Transscription," Vienna, 1863; "Physiologie der Farben für die Zwecke der Kunstgewerbe bearbeitet," Leipzig, 1866; "Vorlesungen über Physiologie," 3d edition, 1881; "Ueber die Ursache der Gerinnung des Blutes"; "Ueber das Vorkommen von Zucker im Harn gesunder Menschen"; "Ueber den Verlauf der feinsten Gallengänge"; "Ueber einige Consequenzen aus der Young-Helmholtz'schen Theorie"; etc. (Pagel.) A. H. B.

Bruise.—See *Wounds.*

Bruits.—It can hardly be said that there is any independent literature in French upon this subject, nor is there much harmony concerning the class of sounds entitled to this appellation. The word *bruit* (French for noise) is used arbitrarily for any sound made within or upon the body, whether spontaneous or induced, whether heard by the naked ear or stetho-

scope, and whether normal or as pathological. It also includes subjective sounds, such as tinnitus aurium. But sounds heard upon percussion (French *sons*) are not spoken of as bruits, although they might be classed under induced auscultatory sounds, especially when so-called auscultatory percussion is used. On the other hand, many heart or vascular sounds are commonly termed *souffles* by the French. A study of the sounds most familiarly known as bruits, which obtain moreover in languages other than French—either as literally borrowed terms or as translations—teaches us that these are descriptive in character and often so through being likened to familiar sounds of every-day life. Bruits occur anywhere in the body but most of them are known as incidents of auscultation of the chest. Others are connected with the stomach and intestine, uterus (placenta), and cord, etc. The term bruit may be applied to any of the râles and rhonchi heard in the lungs, as *bruit de craquement* for the crepitant râle, *bruit de frottement* for the ordinary friction râle produced by inflamed serous membranes. In connection with the heart and large vessels some authors use the term bruit instead of souffle, since bruit is applicable to any sound whatever, while souffle has a more definite significance. Hence, also the two may be used as synonymous, or the word souffle may be general and bruit individual.

Since any auscultatory sound may be rendered in French by bruit it is manifestly not worth while to enumerate them all, and we select for brief consideration chiefly those which are likened to familiar noises. Thus of respiratory bruits we may enumerate:

B. d'airain (brassy sound), obtained by auscultation over a thoracic cavity. It has been likened to the tinkling of a bell.

B. de pot fêlé (cracked pot sound), obtained likewise by auscultation of pulmonary cavities.

B. de drapeau (literally flag-sound), due to the flapping of false membrane or a polypus, etc., in the air passages.

B. de grelot (literally sound of a sleigh-bell), due to presence of a foreign body in the lung.

To the preceding may be added certain pleural sounds of respiratory origin, which have also at times a wider range of application, *e.g.* to the pericardium:

B. de cuir neuf ("new leather" sound, or squeak), a friction sound indicating pleurisy or pericarditis.

B. de craquement (crackling), also heard in pleurisy and pericarditis.

B. de frôlement (rustling), likewise heard under the same circumstances.

These three terms represent special sounds while as already stated the term *bruit de frottement* is the general term for friction sounds. Another may be added here:

B. de moulin (mill wheel sound), a splashing said to occur in pericarditis.

Aside from the souffles many sounds proceeding from the heart and vessels are known outright as bruits, because they have nothing in common with the blowing, murmur-like quality of the former. Here belong:

B. de choc (impact), heard in association with the second sound of the heart in cases of aneurysm.

B. de diable (a humming top), heard in anemia over the veins.

B. de galop (galloping sound), heard in mitral stenosis.

B. de lime (filing sound), accompanying certain heart sounds.

B. de scie (sawing sound), analogous to preceding.

B. de parchemin (sound like that produced by friction between pieces of parchment), a valvular friction sound.

Other valvular sounds have been likened to various noises as the mewing of a cat (*b. de miaulement*), the sound of rasping (*b. de rape*), the sound of a drum (*b. de rappel*), etc.

Bruit de souffle or bellows murmur belongs properly under the souffles.

The extrathoracic bruits most familiarly known are as follows:

B. de clapotement (splashing sound), induced by pressure on the dilated stomach containing fluid.

B. de Leudet, a fine crackling sound in the ear both subjective and objective, the patient usually suffering from an inflammatory or neuropathic affection of the ear.

B. placentaire is a souffle. It is heard over the placental site in the uterus and proceeds from the fetal vessels.

Other bruits are often mentioned, as the *aneurysmal b.*, the *systolic b.*, etc., which are really souffles. Vague general expressions like *b. de froissement* (clashing sound), *b. de claquement* (clapping sound) are used at times for descriptive purposes. The term *false bruit* is used for sounds produced by friction of the stethoscope on the chest and for entotic sounds heard by the auscultator. To include here all the bruits mentioned by French writers would serve no purpose. Those already given are intended for identification only. Their full significance will be considered under *Diagnosis, Physical.*

EDWARD PREBLE.

Brumfels, Otho.—Born at Mainz, Germany, toward the end of the fifteenth century. He studied theology and philosophy early in life and then entered a monastery for a short time. When the doctrine set forth by Luther began to find adherents throughout Germany Brumfels gave up his monastic life and devoted himself for a short time to teaching school in Strasburg. In all his available leisure moments he studied the writings of the Greek and Arabian physicians, and was thus enabled to pass successfully in 1530 the examinations for the degree of Doctor of Medicine required by the University of Basel. Almost immediately afterward the authorities of Berne invited him to practice his profession in that city, and he accepted the invitation. But his residence in Berne was of short duration, for he died there on November 3, 1534.

Notwithstanding the shortness of his career Brumfels managed to win the general esteem of his fellow citizens. To him also must be accorded the merit of having been one of the men who were chiefly instrumental in placing the science of botany upon a sound and durable basis. The titles of his published writings, some of which did not appear in print until quite a long time had elapsed after his death, are as follows: "Catalogus illustrium medicorum, etc.," Strasburg, 1530 (this is said to be the first time that any attempt had ever been made to publish a work of this character); "Herbarum vivæ icones ad naturæ imitationem summa cum diligentia et artificio effigiatæ, etc.," three volumes, Strasburg, 1530–1540 (Haller says that the accompanying plates are quite good); "Theses seu communes loci totius rei medicæ, et de usu pharmacorum, etc.," Strasburg, 1532; "Iatrium medicamentorum simplicium, etc.," two volumes, Strasburg, 1533; "Onomasticon medicinæ omnia nomina herbarum, arborum, etc.," Strasburg, 1534; and "Epitome medices ex gravisimis auctoribus summam totius medicinæ complectens," Antwerp, 1540. (Dict. Hist. de la Méd.) A. H. B.

Brunner, Johann Conrad.—Born on January 16, 1653, in Diessenhofen, near Schaffhausen (now a Swiss town, but at that period belonging to the German Empire). Brunner pursued his medical studies at Strasburg for four years and received the degree of Doctor of Medicine at the early age of nineteen. He next visited Paris, where he continued the study of anatomy with great assiduity, receiving from Duver-

ney, the celebrated anatomist, much encouragement in his work. After leaving Paris he went first to England, then over to Holland, and finally back to his home in Germany. He engaged in the practice of medicine and soon acquired a great reputation; many kings and princes coming to consult him for their ailments. In 1687 he was made Professor of Medicine at Heidelberg. He died at Manheim on October 2, 1727. (Dict. Hist. de la Méd.)

It was Haller's judgment that Brunner was one of the clearest thinkers of the seventeenth century. He demonstrated, by a series of very difficult experiments, that animals can dispense with a pancreas, and that the fluid which it secretes is not essential to life. He was the discoverer of the pituitary body and of the duodenal follicles which still bear his name. Of his writings the following deserve to receive special mention: "Experimenta nova circa pancreas, etc.," Amsterdam, 1683; "De glandulis in duodeno intestino detectis," Heidelberg, 1687; "De glandula pituitaria dissertatio," Heidelberg, 1688. A. H. B.

Brunonian Movement.—See *Brownian Movement.*

Brunonianism.—The "stimulation theory" of disease and its treatment, as formulated and taught for years by John Brown, a Scottish physician (1735–1788). To state that it originated with him would be to err. Brown was never a clinician and could not have built up a doctrine based on years of observation of disease. The essentials of his propaganda are doubtless to be found in Haller and in Cullen, his preceptor. Reduced to their lowest terms they are somewhat as follows: Organs are irritable, respond to stimulation; overstimulation may produce the sthenic diseases, which should be treated by methods of depletion (then in universal use); but organs become exhausted in various degrees as the result of continued stimulation or overstimulation; and practically the great majority of diseases are asthenic in type, requiring instead of depletion supporting measures.

In Great Britain Brown was never regarded as a medical pioneer. His income was derived from tuition fees rather than from patients. A brilliant scholar, thinker, and controversialist he sought to build up a personal following. He turned his back on the faculty and would gladly have founded, if not a sect, at least a school, to champion his views. The "psychological moment" in Brunonianism was when in 1778 he published his "Elementa Medicinæ" in elegant Latin. This work quickly won him a reputation on the Continent where his personality was unknown. Among the innumerable physicians who absorbed his teachings were such leaders as Girtanner in Germany, J. P. Frank in Austria, Rasori in Italy, and Rush in America. For many years a goodly share of the profession throughout the world made use of his formulæ in the diagnosis and treatment of disease. Even to-day in the absence of other views his doctrines could be developed into a respectable working hypothesis. They rest upon no basic fallacy and represent a sound empiricism and common sense. For that very reason, doubtless, they have become so completely incorporated into the medical lore of the ages that Brown's very name is to-day unknown to the rank and file of the profession. Edward Preble.

Bryonia.—The root of *Bryonia alba* L. and *Bryonia dioica* L. (fam. *Cucurbitaceæ*). There are eight species of Bryonia, natives of the Mediterranean region. The *B. dioica* grows as far north as England. They are tendril-bearing, cucumber-like vines, with very large, starchy roots, growing mostly in sandy soil. Their bitter and active constituents are doubtless for the protection of their nutritious roots against foraging animals.

The roots are sliced, mostly transversely, to facilitate drying. These commercial slices are white discs (becoming gray with age), from one to four inches in diameter and one-fourth to nearly one-half inch in thickness. They are not appreciably thinner at the center, though the bark is slightly broader than the fleshy portion. There are several concentric circles of short wood bundles. The surface is granular and slightly harsh to the touch. The fracture is short and sharp. There is a characteristic, though faint odor, and a powerful and disagreeable bitter taste. It is not adulterated.

Composition.—With much starch and gum, and some sugar, the active constituents are the two bitter glucosides *bryonin* and *bryonidin.*

Action and Uses.—Bryony is a hydragogue cathartic, practically identical with colocynth and elaterium. Like these, also, it is a stimulating or irritating diuretic, and thus emmenagogue, for which latter purpose it has been much employed. It is poisonous in overdoses. A ten-per-cent. tincture was formerly official, the dose being ʒij.–iv. (8.0–15.0). The extract, dose gr. iij–vi. (0.2–0.4), is a preferable form of administration. H. H. Rusby.

Bubo.—This term, derived from *βουβών*, the groin, was originally used by medical writers of antiquity to designate glandular tumors of the groin, but was applied by authors of the period of the Reformation to glandular inflammations of every part of the body irrespective of their nature. Modern writers have again reserved the term for inflammatory affections of the lymphatic glands of the groin. While buboes are alluded to in the earliest medical treatises of which we have any knowledge, and the pathogenetic importance of the genitalia in their causation was apparently familiar even to Hippocrates, the distinctive types of the affection which are now generally recognized were, or course, unknown until long after the general outbreak of syphilis, which appeared at the close of the fifteenth century. Then, besides the adenitis, which suppurates and often leaves an ulcer, there presented itself a bubo which from its inception is indolent, unattended by pain, and rarely the seat of suppurative change. Gaspard Torella, Fallopius, Nicolaus Massa, Paracelsus, and other writers of that memorable epoch in the history of venereal diseases speedily recognized and described with sufficient accuracy this earliest systemic manifestation of syphilis. Nevertheless, the nature of buboes was so little comprehended that they were regarded as sympathetic in character, or as unsuccessful endeavors of nature to check through them the invasion of the system by the disease. That the majority of buboes result from the deposit in the lymphatic glands of a poison conveyed to them from a distance could not have been known prior to the discovery in 1651, by Olaüs Rudbeck, of lymphatic vessels situated in different parts of the body and possessing a function of absorption like that of the lacteals previously described by Aselli. Even then precise knowledge of the subject was slowly developed, and it remained for the observations of Hunter, Swediaur, Benjamin Bell, and Ricord to depict the clinical symptoms and finally establish the etiological relations of the different varieties of the disease under consideration.

Anatomical and Pathological.—The subcutaneous cellular tissue of the groin encloses, together with the superficial blood and lymphatic vessels, a varying number (eight to twelve) of lymphatic glands, which receive their lymph from the subumbilical segment of the anterior abdominal wall, from the external genitalia, urethra, perineum, vagina, cervix uteri, anus, and inferior extremity. The size of the inguinal, as of other lymphatic glands, in their normal state is so small that in persons with a panniculus

adiposus of ordinary thickness they cannot be felt through the skin. Oval or elongated in form, the glands of the groin are arranged in two quite distinct groups, the larger of which follows the course of Poupart's ligament, while the smaller forms part of the cribriform fascia covering the saphenous opening. The individual glands of these groups, when naturally large or enlarged from disease, present distinctive directions. Those which overlie the ligament have their axes parallel to the inguinal fold, while those of the lower group have their axes parallel to that of the lower extremity. This factor is of considerable importance, in that it often gives a clue to the source of the ganglionic complication, since the lymph from the external genitalia is conveyed to the upper, while that from the lower extremity passes to the lower chain. It must not be forgotten, however, that these groups communicate very freely with each other by numerous lymphatic vessels, in which the circulation is from the upper to the lower glands. Indeed, it is through the glands over the saphenous orifice and through one or two glands (Rosenmüller's) deeply seated underneath the fascia lata, that the lymph must pass from both lower extremity and genital area before it can enter the general lymph receptacle in the abdomen, after passing through the retroperitoneal iliac nodes. This anatomical factor will account for the not very infrequent occurrence of two suppurating glands on the same side of the body, of which one belongs to the upper and the other to the lower chain, the inguinal fold lying between them. This will account also for the very rare instances of retroperitoneal suppurative lymphadenitis as a result of a chancroidal inflammation of the external genitalia.

Formed of a capsule embedded in the periglandular adipose tissue, containing within it lymph sinuses networks of reticular connective-tissue, and lymph cells, the lymphatic gland, when the seat of inflammatory changes, presents appearances which vary greatly with the degree of the inflammatory process and the nature of the primary cause. The acute adenitis which may follow in the wake of any traumatic or specific infection of the skin or mucous membrane, and which manifests itself clinically by moderate swelling and tenderness of the affected gland, is associated with dilatation of its blood-vessels and proliferation of the lymph corpuscles contained in the meshes of the reticular network or stroma.[1] When this cellular infiltration becomes excessive the reticular net-work suffers from compression; it becomes rarefied, the capillaries are obstructed and practically obliterated. When deprived of their nutrition the infiltrating cell masses are speedily converted into pus foci. Though the confluence of these the gland capsule, already distended from the inception of the process, becomes an irritant to the surrounding parts; the subcutaneous cellular layer and the skin more or less rapidly participate in the morbid changes, and soon the suppurating bubo, having attained twenty fold the size of the normal gland, is emptied spontaneously or by the knife of the surgeon. After the evacuation of the pus the abscess cavity speedily contracts, and cicatrization ensues with such rapidity at times that the wound is closed in a week from the opening of the bubo. Not always does this process of repair follow so quickly the elimination of the pus. The behavior of the periglandular tissue is a most important factor in the events that are to follow. This is often the seat of more extensive inflammation than the gland itself. Minute abscesses form around the inflamed gland from obstruction of its afferent vessels, so that after the elimination from the gland itself this remains embedded in a secondary abscess cavity formed about it. Covered by granulations it may in time appear as a foreign body in the floor of an ulcer, or it may remain for months covered by integument but surrounded by indolent sinuses. Nor is the pathological process that ends in suppuration necessarily limited to one gland alone. The infection may be conveyed from the gland originally involved to one or more in the vicinity, until a number of them are bound together in one large inflammatory mass, the suppuration of which usually entails the destruction of a considerable extent of skin. To a large extent, the termination of an adenitis depends upon the nature and gravity of the primary disease. If the infection in the lymph radicles of the affected gland is mild or evanescent, as in herpes, balanitis, erysipelas, or gonorrhea, the consecutive adenitis rarely proceeds to suppuration. Absorption of the infiltrating cellular elements may supervene in a few days or even hours. On the other hand, long continuance of the local irritation, whatever its character, will at times completely change the results of the glandular inflammation in that the cellular infiltration, being insufficient in extent to induce suppuration, yet not disappearing by absorption, leads to organization. Here it is not the exuded lymph corpuscles that are converted into a durable tissue, but the reticular substance which forms the framework of the gland. In the suppurating adenitis this disappears; in subacute adenitis it undergoes a reactive hypertrophy. In the course of time the septa of the gland increase so greatly in thickness that the lymph corpuscles between them are seriously encroached upon. Hence the firm fibrous appearance of the section of a lymphatic gland that has been the seat of a chronic inflammation.

Etiology and Varieties.—The inguinal glands differ in no way from those of other parts of the body, and the morbid processes to which they are subjected can be duplicated in those of the groin. Hence *a priori* reasoning as to the venereal origin (using the term in its widest significance) of an adenitis here situated must be strenuously deprecated. Violent exercise, strains while lifting or while mounting a horse, direct trauma, herpes, furuncles, eczema genitalium, and scabies may all be the source of an inguinal adenitis. Some time ago there appeared at my clinic a lad of seven years, with two suppurating glands, the one above, the other below the ligament. The most careful inspection of genitalia and lower extremity failed to reveal anything abnormal. The cervical glands were not enlarged, nor were there traces of tuberculosis or syphilis discernible. The only adducible cause of the bubo was a severe fall from a sand bank, which the boy had sustained one week before aggravated symptoms supervened. Buboes such as these, which in no way depend upon an inoculable, undiscoverable primary disease, and which stand neither immediately nor remotely in connection with the sexual act, I have been in the habit of designating *non-venereal buboes*.

Each of the three typical venereal affections, viz., gonorrhea, the chancroid, and the initial lesion of syphilis, may be attended by complications of the inguinal glands, which are known as *venereal buboes*, and are subdivided into, (1) the simple or inflammatory; (2) the virulent, and (3) the syphilitic varieties. They are produced respectively (1) by the irritation of a gonorrhea and chancroidal or syphilitic ulcer; (2) by the chancroid solely, and (3) by the presence of the initial lesion alone.

1. Buboes are rarely produced by gonorrhea. While a slight tenderness of the neighboring glands not infrequently attends a urethral discharge, it is very exceptional to witness in them an inflammation that ends in suppuration. Perry[2] states that in the United States Marine Hospital Service two and one-half per cent. of gonorrheas are followed by suppurating buboes. In 327 cases of gonorrhea seen by Sigmund, suppurating buboes developed in 19. Yet buboes of considerable size, with extensive destruction of tissue, are occasionally encountered as complications of gonorrhea. They have been met mostly in very young subjects, in persons of tubercu-

lous habit, or in subjects debilitated by a previous attack of syphilis. Again, it is not unusual to find a chronic hyperplasia of one or more of the inguinal glands after repeated and prolonged urethral discharges, a condition analogous to that of the cervical glands in persons prone to catarrhal affections of the throat. The term "sympathetic bubo," formerly applied by preference to gland complications of gonorrhea, is gradually being discarded. Whether the bubo results from purulent preputial catarrh. gonorrhea, or chancroid, instances are not rare in which there can be detected that cord-like swelling along the dorsum of the penis which is but the evidence of a lymphangitis developed by direct propagation of the disease from its first seat. Still, the morbid process in the lymphatic vessels does not usually manifest itself by perceptible symptoms. Like the vas deferens in epididymitis, the lymphatic vessels convey the irritant to the gland without being often seriously affected by it.

2. The chancroid is by far the most common precursor of the bubo. From its very inception to the period of its repair, and even for months after its complete closure, the chancroid may be the cause of an inflammatory bubo. This the soft sore may accomplish in its dual capacity of harboring the ordinary pus-formers and the special bacillus of Ducrey and Unna. Ricord formulated the law that when the chancroidal virus is absorbed into a lymphatic gland there must inevitably be a suppurating bubo, the pus from which, in turn, will reproduce a chancroid. When the pus from a bubo of chancroidal origin is not inoculable, it is presumed that the fluid absorbed from the chancroid did not possess the characteristic qualities of chancroidal virus. This is the distinguishing feature between the simple and virulent buboes originating in chancroids. Still, it is difficult to comprehend why a large, suppurating, yet non-virulent bubo should follow from the irritation of so small an area as is usually covered by a chancroid, when it so rarely follows the infinitely more extensive irritation of the urethra from gonorrhea. It has been estimated that the proportion of simple to virulent buboes (following chancroids) is nearly equal; it being 149 simple to 138 virulent.[3] These figures are far from conclusive, since every case should be made the subject of most careful inoculation before being utilized in statistics. The relative frequency of buboes in general as a complication of chancroids has been more accurately determined. Fournier[4] has observed 207 chancroids of which 65 were complicated by suppurating buboes.

In 146 cases of chancroid observed at my dispensary in the Medical College of Ohio, during a period of two years, suppurating buboes were recorded in 40. Thus it appears that in about twenty-eight per cent. of the total number of chancroids buboes appear. In private practice the proportion is not so large, since with proper treatment of the primary ulcer ganglionic infection can generally be averted. It is a remarkable fact that in women buboes are not so prone to develop as in men, owing probably to the fact that the latter cannot abstain from work for a trivial soft chancre. The size of the original sore does not appear to influence, in any manner, the action of the inguinal glands, since it is not unusual to find destructive buboes following small and superficial ulcers, while destructive chancroids remain uncomplicated. The retention of the discharge from the chancroid is, no doubt, an important element in the production of buboes, since those of the frenum and those associated with phimosis are relatively most often followed by them. With few exceptions the chancroidal bubo develops in the groin of the same side occupied by the first sore. When this is situated in the median line, and particularly when it involves the frenum, bilateral buboes are apt to supervene. Only in very exceptional cases is the irritation or virus conveyed across the median line, to the glands of the opposite side, through the anastomosis of the lymphatic vessels. Occasionally a bubo will form in the median line at the root of the penis, or in the pubic region, where a small lymphatic gland is often found at the confluence of the lymphatic vessels of the two sides. Pubic buboes were encountered in three out of 298 cases.[5]

The pus from chancroidal buboes is ordinarily sterile and free of microorganisms. Inoculation with it as a rule fails. This has been shown by Strauss, Spitscka, and others. The most extensive investigations relative to this question have recently been made by Deutsch.[6] He examined the pus from sixty-six buboes. Thirty-seven occurred with the soft sore, twenty-nine with the hard or mixed ulcers. Bacteriological experiments were made with a view to establish autoinoculability, and to determine the length of time required for the bubo to heal. Of the thirty-seven cases occurring with the chancroid, inoculation upon the abdomen with the production of a typical chancroid was successful in only three cases. In these three cases the pus from the bubo showed the Ducrey bacillus. The pus from chancroidal buboes could be classified under three categories: (*a*) Sterile pus; (*b*) pus containing ordinary pyogenic microorganisms; (*c*) pus containing the Ducrey bacillus with or without the admixture of other microbes. In the twenty-nine cases occurring with the hard or mixed sore, autoinoculation was successful in only three cases, and in only one was a typical hard sore produced. It may safely be stated, therefore, that in the great majority of cases suppuration in buboes is the result of toxic absorption, and is not due to the entrance of microorganisms themselves into the lymph channels and nodes.

3. The initial lesion of syphilis is almost invariably followed by a sclerosis of the upper chain of the inguinal lymphatic glands, of which the innermost is first involved during the first fortnight after the primary sore manifests itself. In the course of a few weeks the other glands of this region (*pleiades ganglionnaires*), and subsequently the glands in general, become affected. Fournier failed to find induration of the inguinal lymphatics five times in 265 cases; Berkeley Hill[7] three times in 176 cases; whereas Bumstead[8] has never "met with a chancre which was not attended by induration of the neighboring lymphatic ganglia." It is a characteristic of the syphilitic bubo that it involves the entire chain of lymphatic glands, and that its progress is not attended by acute symptoms. Hence this form of bubo is often termed *indolent*. In its morbid anatomy nothing of an inflammatory nature is apparent. The small-celled infiltration which takes place in the initial lesion of syphilis is reproduced in the inguinal glands. Every mesh of the reticulum is fully distended by cells. The induration resulting therefrom continues for months, and even for years, without terminating in inflammation or necrosis of the gland. As in the case of the primary induration, after continuing for a varying length of time, a fatty metamorphosis of the cells ensues; the detritus is absorbed, and the gland returns to its normal condition (Rindfleisch).[9] In galloping syphilis and in that of tuberculous, and particularly young subjects, the inguinal glands at times undergo extensive suppuration. Even then it will be found that the immediate cause of the inflammation is a secondary pus infection of the primary ulcer, with the developement in it of phagedena. This suppuration of an indolent bubo, therefore, has neither a favorable nor a contrary influence on the subsequent course of the syphilis. While the suppurating adenitis is, as a rule, a sequel of the soft chancre, its presence does not infallibly demonstrate the non-infecting (chancroidal) character of the primary sore.

Bubon d'Emblée.—The buboes which have been thus far considered are ascribable to plainly discernible

lesions in the area of origin of the lymphatic radicles of the affected gland. Therefore they are secondary in character. The question has for a long time been discussed whether, without the development of a lesion at the point where the virus entered the body, this could be directly absorbed and conveyed to the glands and produce in them its peculiar pathological effects. Authorities of great weight (Vidal, Reynaud, Benjamin Bell) have cited numerous instances in which such absorption without local reaction is supposed to have taken place. To designate this particular form of ganglionic disease the terms "primary bubo," "idiopathic bubo," and "bubon d'emblée" have been used as synonyms. It has already been observed that primary buboes could arise from direct trauma, excessive exercise, strumous habit, and other like causes. Aside from these etiological factors, it is at present deemed impossible for a venereal bubo to develop without preexisting primary trouble. It is within the experience of every one that this primary affection may be very trivial in extent and of remarkably short duration, therefore escaping the attention of the patient. Here, as in the case of the minute dissecting wound that may lead to suppurating lymphadenitis, and even to death, the original lesion, or some trace of it, can always be found. Until it can be demonstrated that chancroidal pus or syphilitic virus can be made to permeate the unbroken skin, there is no good cause for believing in the bubon d'emblée. It is particularly through the efforts of Ricord, Langlebert, Fournier, and others that the "idiopathic bubo," for so long a period the subject of most ardent polemics, is now generally believed to have no actual existence.

Symptomatology.—*Simple Bubo.*—The appearance of an inguinal bubo is ordinarily announced by a feeling of discomfort while walking. A passing sense of fulness causes the patient to examine the part, when he finds one or more tender glands in the groin. Palpation at this time reveals the presence of a resistant, movable swelling, tender to the touch, and varying in size from a bean to a cherry. Within a few days the symptoms rapidly increase in severity. The tumefaction, increasing in extent, is oblong in form with the long axis parallel to the groin when a gland of the upper chain is affected, and parallel to the axis of the thigh when one of the lower group is involved. A decided elevation of the skin becomes apparent before its implication in the process occurs. Pain is usually complained of, and it is either sharp and spasmodic in character or dull and constant. Hence follow disturbed sleep and impeded progression. With the extension of the inflammation to the periglandular tissue, the mobility of the swelling disappears, the tumor loses its well-defined outline, the skin itself becomes adherent and the seat of more or less redness. Even when symptoms so pronounced as these have continued for a week or more, resolution may supervene in the course of two or three days. Such a fortunate termination is more likely to ensue when the primary affection was a gonorrhea, balanoposthitis, or herpes. But in undoubted cases of chancroid a gradual resolution of the acute inflammation, or its termination in a chronic induration, is not at all infrequently observed. These terminations are quite as likely to follow in the buboes which supervene during the early stages of the chancroid as in those that attend the reparative process of the sore or that follow its cicatrization.

When the inflammation passes to the suppurative stage the indurated mass generally presents a softer spot, which is as often situated out of, as in, the center of the swelling. With the increase of the area of softening the skin changes to a dusky hue. An examination, while the skin is still intact, reveals distinct fluctuation, and when the attenuated integument is indented by the finger the indurated wall of the abscess can ordinarily be distinguished. It is at this time, from ten days to two weeks after the beginning of the bubo, that the pus is usually evacuated by incision. In quantity this does not often exceed an ounce. If left to itself, weeks will often elapse before the skin undergoes pressure necrosis, during which time the abscess increases in its dimensions until it contains at times from four to six ounces of thick, creamy pus. When permitted to open spontaneously, the abscess usually opens at one point only, although two or three apertures are often formed. This feature of inguinal suppurating buboes requires especial mention. When the swelling has attained the size of a walnut or small peach, it will often appear to be subdivided by a deep furrow into two quite distinct growths, of which the smaller is usually situated below and nearer the median line. When suppuration is finally established, a separate opening will be formed or made necessary for each division of the swelling, irrespective of the question as to whether more than one gland is involved. Not always does the suppurating bubo run so acute a course. Instances are not at all infrequent in which the inflammatory symptoms develop in successive stages with intervals of quiescence. Such buboes often require several months before maturing, and for these cases the term "subacute" is occasionally reserved. The pus contained in them is usually watery in character, and ordinarily not very abundant.

The clinical course of a simple bubo, after it has discharged, does not differ materially from that of an abscess from other causes. In about thirty per cent. of all cases, and particularly in those in which an early incision was made, the walls of the abscess become agglutinated, and suppuration rapidly ceases. Generally, however, the discharge continues for from one week to many months before the abscess cavity is obliterated. Chronicity of discharge characterizes particularly those abscesses in which more openings than one have formed, and in which sinuses lined with exuberant granulations undermine the skin. In many of these cases, the force of the inflammation having been spent on the periglandular tissue, these sinuses lead down to one or more glands. When the integument covering the sinuses finally yields to the suppurative process, or is divided by the knife, the gland covered by granulations will appear in the floor of the ulcer or in the wound thus produced.

Virulent Bubo.—With the conveyance of the ptomaïnes or of the specific microbes from the chancroid to the lymphatic gland, suppuration in the latter is inevitable. The bubo of absorption, which results from this, in its inception presents symptoms precisely like those that belong to the simple bubo. The rapidity of development of the symptoms alone might arouse suspicions as to the virulent form of adenitis. It is only after the evacuation of the abscess that the differential diagnosis becomes practicable. Inoculation with the pus of the virulent bubo invariably produces a chancroid; inoculation with the pus from a simple bubo yields negative results save in syphilitic subjects (*vide supra*). But the inoculation test is superfluous, since the progress of the virulent bubo after it is opened is usually sufficiently pronounced. The margins of the wound which gave passage to the pus become inoculated with the chancroidal virus. As in the chancroid, during its period of progress the integument covering the virulent bubo is rapidly destroyed until a true chancroidal ulcer, varying much in area and depth, presents itself in the groin. When fully exposed to view, the floor of the bubo, from absorption, presents the yellowish-gray, irregular, and worm-eaten appearance of the chancroid. The margin of the ulcer, tumefied at one part, appears attenuated or undermined at another. From the entire surface there is exuded a watery pus which is often tinged with blood. Capillary hemorrhages

from the bubonic ulcer are often encountered as in the chancroid. Indeed, the clinical history which belongs to the chancroid is on a larger basis duplicated in the case of the bubo. Healing in rare instances in a few weeks, in less fortunate cases it continues in its destructive course for months, and occasionally even for years. When thus protracted, the ulceration usually assumes the serpiginous type, healing in one portion and extending in another. Thus the ulcer gradually spreads over abdomen, thigh, pubes, or gluteal region, leaving frequently ungainly cicatrices. In these cases the ulcerative action is often so sluggish that, as in lupus or rodent ulcer, it is almost imperceptible. Continuous autoinoculation of the skin in the vicinity of the ulcer is the only plausible explanation of these protracted forms of bubo. Phagedena, that most terrible complication of the venereal sore, occasionally attacks the virulent bubo. Under its influence the bubo may in a few weeks become converted into an ulcer the size of the palm. Superficial in some cases, in others the ulcer under its influence dips down into the tissues, producing extensive sloughs. Progressing among the blood-vessels, it has been known to open them and induce fatal hemorrhage. Fatal results have likewise been induced by the excessiveness of discharge and from generalized septic infection.

Syphilitic Bubo.—The inguinal adenopathy of syphilis is but the reproduction on a larger scale of the indurating process manifested in the primary lesion. Appearing early and affecting an entire group of glands, the syphilitic adenopathy yields a row of larger and smaller tumors, freely movable and easily felt, except in very obese subjects. These tumors are hard, resistant, not tender to the touch, and usually largest on the side of the primary sore. Oftener than in the other forms of bubo, the dorsal lymphatics of the penis participate in the morbid process and appear in the form of indurated cords with irregular nodosities. Like the enlarged lymphatic glands, these lymphatic cords are freely movable. It has already been observed that indolence characterizes the syphilitic bubo. Only in persons of tuberculous taint, and in cases of great malignancy of the syphilitic virus (galloping syphilis), does suppuration ensue. With or without treatment, the syphilitic bubo continues while the primary and many of the secondary manifestations remain. It is rare to find these buboes subside completely, even under treatment, in less than two or three months, and in many instances they survive all other syphilitic lesions, when they assume great diagnostic importance in determining the presence or absence of a syphilitic taint. After continuing sometimes in an unaltered state for two or three years, they finally subside spontaneously.

Treatment.—The treatment of buboes must necessarily vary with the nature of the primary trouble. In a prophylactic way nothing can be done to prevent the syphilitic bubo, while much can be accomplished in the prevention of simple glandular inflammations as complications of the chancroid and gonorrhea. In both these affections violent exercise and excessive walking and riding should be strictly interdicted. Irritant applications to the primary disease should be strictly avoided, since too astringent urethral injections and irritating ointments applied to chancroids are often the immediate causes of gland complications. What influence has the cauterization of the chancroid upon the development of buboes? If statistics be carefully examined, it will be found that in about thirty per cent. of all cases buboes supervene, and that their development is uninfluenced by the use of, or abstention from, cauterization. For this reason the application of violent caustics to chancroids is being more and more discarded. Of much greater importance as a prophylactic is cleanliness and the securing of a free escape for all discharges. It is for this reason that chancroids treated in private practice are much less often complicated by buboes (according to my experience, one to eight) than those of hospitals, and particularly of dispensaries.

When the evidences of an adenitis become unmistakable, every effort must be made to bring about resolution of the inflammation, since this favorable termination is possible in every instance save those in which the chancroidal virus has been observed. As in other inflammations, rest in bed is the chief antiphlogistic measure, and its importance must be fully explained to the patient. Applications of very cold cloths will at this time prove serviceable. A rubber bag is preferable, since it acts at the same time as a compressor. Local applications of the liquor plumbi subacetatis, with cold compresses, have been highly recommended by Hamilton and Zeissl, and are doubtless often beneficial. It is at this period of the inflammation that repeated applications of the tincture of iodine are so frequently resorted to. Although this practice has stood the test of time, and has the sanction of eminent authorities, it seems to me devoid of benefit and often pernicious in its results, since it not infrequently is followed by violent inflammation of the skin and hair follicles, even to the extent of vesication. Another important objection to the tincture of iodine is the fact that the artificial condition of the skin produced by it frequently prevents the early detection of suppuration. When, for the purposes of absorption, iodine seems indicated, I have lately employed the iodide of lead quite extensively, using in connection with it veratrine, belladonna, or opium to allay pain. Inunction with iodine-vasogen, six per cent., likewise serves a good purpose. Inunctions with Credé's ointment or with preparation of collargol or guaiacol may often be used with good results. Since compression, where it is practicable, plays an important rôle in the treatment of inflammations, it should be used here. It can be best applied by means of a bag half-filled with small shot. If the patient cannot be retained in bed, collodion applications and a compress, held in position with a spica bandage, should be resorted to. Happily for the patients, a number of methods of aborting the inflammation which were formerly practised have been entirely abandoned. Among them may be mentioned methodical compression by instruments, repeated blistering with the subsequent application of mercurials, the forcible rupture of the gland capsule, and the use of the seton. To these may be added the subcutaneous incision of the gland and the somewhat analogous procedure of Auspitz. The latter observer punctures the inflamed gland even before suppuration can be detected. A probe is introduced through the opening and the glandular septa are torn; the substance of the gland is thus broken up and discharges through the external wound. This practice of Auspitz has not found and does not deserve many followers. Nevertheless, it has been most highly indorsed by Bumstead. Intraglandular injections of iodoform emulsion, carbolic acid, and corrosive sublimate have been used to avert suppuration. Welander[10] advocated the injection of a one-per-cent. solution of benzoate of mercury. Of seventy-eight cases reported, fifty-six were cured without suppuration. Perry[2] employs it in all non-suppurating buboes, injecting twenty to thirty minims of the solution. More than two injections are rarely necessary and the time required to effect a cure is fourteen days.

When suppuration has been established, the treatment of the bubo must not vary from that of abscesses in other easily accessible portions of the body. *Ubi pus, ubi incisio* is a rule that should be adhered to in the disease under consideration. The ways in which the pus is to be evacuated are numerous. Within

the last fifteen years aspiration has often been resorted to, and has been highly recommended by a number of French and German observers. When it is evident that the purulent accumulation is small, and that a suppurative periadenitis has not yet developed, aspiration cannot be too often practised. Attended by little pain, it can do no harm, and is sometimes followed by permanent agglutination of the abscess walls. Among recent writers R. Hahn speaks most favorably of it. In a series of 200 cases, seventy per cent. were cured by aspiration alone. In three-fourths of the cases one aspiration sufficed.[11] When the abscess is large and the skin attenuated, the only hope for a speedy recovery lies in the prompt and complete evacuation of the pus. The use of the Vienna paste, blisters, and multiple incisions to effect this has been properly abandoned. The last-named method, particularly recommended by Vidal, Zeissl, and Langston Parker, and still practised by many older practitioners, is prone to result in the formation of a number of ulcers in the groin. In the great majority of cases, a single incision, with a narrow blade, is all the operative interference called for. Until two decades ago the incision usually made was parallel to the inguinal fold and extended the entire length of the swelling. The result of such an incision is almost invariably a wound the edges of which are in apposition except when the patient is lying down. Again, when ulceration of the margins of the wound ensues, the skin is very apt to become undermined or inverted. Hence very ungainly cicatrices result that might ordinarily be avoided by making the incision in a different manner. A good procedure is the following: The field of operation being prepared in the usual way, local anesthesia is produced by the ether spray or preferably by the Schleich method (see the article on *Anesthesia, Local*). The long and narrow knife, while held perpendicularly to the surface of the body, is then gently forced into the center of the fluctuating area. The skin and capsule of the gland resist slightly the intrusion of the blade. When this resistance has been overcome, the cutting edge of the knife is turned about ninety degrees and then withdrawn. With a little pressure, or by inserting a grooved director into the cut, the accumulated pus rapidly escapes. To prevent a too speedy closure of the opening, it is advisable to insert a strip of iodoform gauze or carbolized gauze within a split tube. This also insures the ready drainage of the abscess cavity. When this is removed, after remaining twenty-four hours, it will invariably be seen that the aperture, measuring from one-eighth to one-fourth of an inch in diameter, is circular in outline, and sufficiently large to permit the escape of the pus as rapidly as it is formed. The after-treatment consists of the application of bichloride gauze fomentations, or the use of the balsam of Peru 10, and castor oil 100, mixture. For cleansing the abscess cavity, injections of hydrogen dioxide may be called for from time to time. Thus treated the bubo usually heals in from ten days to two weeks. As already remarked, the bubo often has a tendency to point at a number of places, when it of course becomes imperative to use the knife repeatedly. The practice of Milton, who uses a very large needle for this purpose, might profitably be imitated in timid patients and by practitioners unaccustomed to the use of the knife. Not so, however, in case of extensive periadenitis and of virulent bubo. When the abscess is very large, a somewhat freer incision is necessary. Even here it seems to me better to make it parallel to the axis of the limb, irrespective of the direction of the bubo. The wound thus made is more easily maintained patent, and in making it there is manifestly less danger of wounding the deep-seated vessels than from the incision as generally made. Almost immediately after opening a large bubo there will be a sinking in of the integument. In the course of a week, or even less, this skin becomes discolored, curled upon itself, or undermined. Under these circumstances it is always best to remove the cutaneous flaps with a few strokes of the curved scissors, thus converting the abscess into an open ulcer. In other cases fistulæ in the groin continue to discharge indefinitely. They should be freely laid open with the knife or elastic ligature, and the exuberant granulations removed with the sharp spoon. When once the bubo has been converted into an open ulcer its treatment is ordinarily successful, no matter what applications be made, although at times stimulating medicaments are called for to overcome the sluggishness of the granulations. Among the large number of agents specially recommended for this purpose there should be mentioned iodoform, tincture of iodine, tannin, permanganate and chlorate of potassium, preparations of iron, and boric acid. Iodoform usually acts so satisfactorily as almost to merit being called a specific in the treatment of the open bubo. Applied in the form of ointment alone, or with tannic acid, or in ethereal solution (iodoform, eight; ether fort., thirty), it soon causes the floor of the ulcer to be covered with small and healthy granulations which rapidly lead to its permanent closure. When the odor of iodoform is an insurmountable objection to its use, the permanganate of potassium (0.5 to 30.0), in aqueous solution, is an excellent substitute. The balsam of Peru dressing already referred to also forms a useful application. When the ulcer has become indolent a five-per-cent. "scarlet red" ointment answers admirably. When the reparative process is exceptionally protracted, from the size of surface involved, skin-grafting has been used with as much success as in other portions of the body.

Attention has already been directed to the fact that the lymphatic gland covered by granulations often presents itself in the floor of the bubonic ulcer, or is hidden in the depths of a sinus. The gland then acts as a foreign body. It should therefore be removed as soon as it is discovered. Whether this is to be accomplished with scissors, ligature, or Volkmann's spoon must be determined by the circumstances of the case and the predilections of the surgeon in charge.

Excision.—With the development of modern methods of wound treatment excision of buboes, which if left alone would probably suppurate, has become a favorite method of treatment. It is not to be recommended as a routine procedure, because of the extent of operation necessary to remove all glands and of the danger of wound infection from the primary ulcer. Furthermore, the time required for cure, averaging thirty days, exceeds that which is needed when conservative measures alone are adopted.

Excision is indicated when infection has taken place in a number of glands and when it is evident that the process of suppuration will be long continued. By free excision in these cases the healing process can be curtailed as to time. Primary union should not be sought for; in most cases it will fail. Very extensive and particularly bilateral excision of the glands is fraught with the danger of lymph-stasis in the regions tributary to the glands removed. As a result there develops a pseudoelephantiasis which of necessity is beyond relief. Very extensive enlargements of the penis and scrotum have been known to follow such extensive excisions. Fig. 1161 illustrates such a case from the service of Dr. Heidingsfeld in the Cincinnati Hospital. The circumference of the prepuce was over eleven inches.

It is self-evident that the systemic treatment of patients afflicted with buboes must not be neglected. Nutritious diet and tonics are always indicated after the process of suppuration has become somewhat protracted. This is particularly true if the ulcer shows any tendency to phagedena. It is then that cod-

liver oil, quinine, and alcoholic stimulants are indicated, and that the most effective local measures must be resorted to. Blisters, fuming nitric acid, the carbosulphuric paste, bromine, and even the actual cautery must at times be employed before the tendency of the ulcer to spread is permanently overcome, and the process of cicatrization is well established. Fortunately, this class of cases is becoming rarer from year to year.

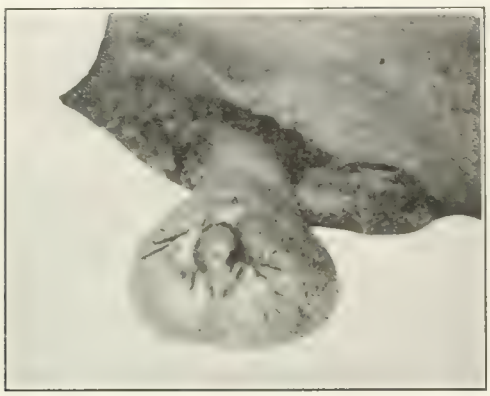

Fig. 1164.—Pseudoelephantiasis of the Prepuce Following Excision of a Bubo.

Syphilitic buboes, as a rule, require no local treatment. As the secondary manifestations of the disease disappear under treatment, the enlargement of the inguinal glands also subsides. When the induration in them persists after other symptoms have yielded to treatment, inunctions with the mercurial ointment or the oleate of mercury over the ganglia will often cause their reduction in size. Compression might also be resorted to in these cases with marked benefit.

Joseph Ransohoff.

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Bubo, Climatic.—An inguinal adenitis peculiar to tropical and subtropical places, and of unknown etiology. The disease is common in the West Indies and tropical America, in eastern and southern Asia, in eastern and western Africa. It is seen with less frequency in other parts of the tropical world and on the coasts and islands of the Mediterranean.

The cause is unknown. There is no antecedent genital lesion or definite urethral infection. In the large majority of cases the affected glands do not suppurate, and cultures of fluid obtained from them by puncture are found to be sterile. In other cases, with or without suppuration, cocci are found in the glands, and occasionally unidentified bacilli. The disease is not *pestis minor* and has no relation to plague. The Wassermann test is negative.

From a considerable experience of his own, and a study of the literature of reported cases, Staff-Surgeon Rost of the Imperial German Navy (*Archiv f. Schiffs. u. Tropen-Hygiene*, Oct. 20, 1912) argues, on what appear to be reasonable grounds, that the disease is probably of venereal origin, and that it is probably due to infection of the surface of the glans in coitus with some undiscovered specific microorganism, more common in the genitalia of colored prostitutes in some tropical regions than in others, and not producing any demonstrable lesion at the point of entrance. The grounds for this tentative opinion are briefly as follows: Under similar conditions so far as climate and exposure are concerned the disease is in some localities common, in others rare, in others unknown. It is common in men, almost unknown in women, common among the unmarried, rare among the married. It is common in men over twenty years of age, very rare in those under twenty, unknown in children. It affects, primarily and commonly the inguinal glands above Poupart's ligament which receive the genital lymphatics, rarely and secondarily the femoral glands. In every one of Rost's seventeen cases he could establish the fact of recent illicit intercourse.

As usually seen the disease has a long period of incubation, appearing in sailors and passengers in from ten days to five weeks after the last visit ashore. The irregular tumor, consisting of a group of glands above Poupart's ligament, well defined below and laterally, is often felt as extending back along the line of the external iliac vessels, its upper limits being lost in the abdomen. Involvement may extend later to the femoral glands. In only a minority of cases periglandular tissue becomes involved in the inflammation. Subjective pain is trifling or absent, but tenderness to pressure is marked. The temperature shows a moderate rise at first but soon becomes normal and there is little constitutional disturbance throughout the case. In its development and its resolution to final disappearance, the bubo runs a slow course of many weeks. At its maximum it may be as large as a goose-egg or larger. Suppuration occurs in a small minority of the cases.

Having in mind the character and course of the disease, climatic bubo must be differentiated from pestis minor; and from other lymphatic inflammations due to filarial infection, to chancroid, or to infected wounds.

During the first two weeks or more, and until the tumor has at least ceased to increase, rest should be enforced, with symptomatic and expectant treatment. The majority of cases do not suppurate and the disease will be self-limited. But when suppuration occurs or appears to be impending the involved glands should be cleanly excised. If merely incised, healing is apt to be slow and there is danger of extension with formation of sinuses and fistulæ. J. F. Leys.

Bubonic Plague.—See *Plague*.

Buchu.—*Short Buchu.* "The dried leaves of *Barosma betulina* (Thunberg) Bartling et Wendland, (fam. *Rutaceæ*)." (U. S. P.) B. *serratifolia* Willd., "Long Buchu," was also once official, but was dropped. It is proposed to reintroduce it in the next edition. B. *crenulata* Hooker, ("round buchu") was also formerly official. There are about fifteen species of this genus, all natives of South Africa. The drug was in use by the Hottentots at the time of settlement by the whites. Its introduction to America was in the form of a notorious quack medicine, but it was afterward adopted upon its merits by the profession.

The leaves of *B. betulina*, the best variety, are mostly one-half to three-quarters of an inch long and two-thirds as broad or more, occasionally broader than long. They are abruptly contracted into a short, narrow basal portion, the broad upper portion being irregularly subrotund, the summit blunt, often recurved, the margin sharply and finely dentate. They are very thick, brittle when dry, smooth and somewhat shining, slightly papillose, and of a yellowish-green color. Against the light they are

pellucid-glandular-dotted, with larger marginal glands. They have a strong mint-like odor and a warm, aromatic, and mucilaginous taste.

B. crenulata varies from oblong to oval or obovate, usually a little broader than in the illustration, and is often twice as long as the other, and less blunt. The margin is crenulate. It is also thick and greenish-yellow, and has similar pellucid glands.

B. serratifolia is markedly different from the others, being of a bright green color, thin, sub-three-nerved by the elongated basal pair of veins, narrowly oblong or lance-linear, sharply serrate, the teeth and sinuses curved. The leaf is about as long as the *B. crenulata*. There is a very large gland at the obtuse summit.

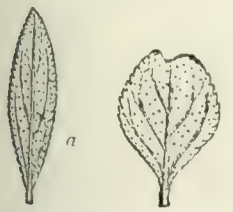

Fig. 1165.—Buchu Leaves. *a*, *B. Crenulata*; *b*, *B. betulina*. (After Baillon.)

There is no adulterant of the official buchu, but when long buchu was official, the leaves of *Empleurum serrulatum* Ait. were sometimes used for that purpose. They are distinguished by the very acute apex and the straight, incised, salient, longer toothing. The chief defect of commerical buchu is the presence of an excessive amount of stems, and the Federal government now forbids the presence of more than ten per cent. The Cape government imposes an export duty on buchu, amounting in 1912 to 2s. 6d. Recently, adulteration has been reported with Agathosma leaves, which have an anise odor, and with Psoralea leaves, which are dotted and hairy, as well as with leaves of other and inferior species of Barosma.

Composition.—Buchu contains 1 to 1.5 per cent. of volatile oil. There are also resin, gum, and a little of the bitter glucoside *barosmin*, believed to be the same as *hesperidin*. The oil contains a camphor-like body, often called buchu camphor (diosphenol $C_{10}H_{16}O_2$).

Action and Uses.—Buchu acts locally as a mild stomachic. Absorbed, it possesses the ordinary diffusive stimulant properties of volatile oils, its special point of action being the kidneys, by which it is excreted. Its diuretic properties are mild, but it is distinctly sedative and astringent to the urinary organs, as well as slightly antiseptic. Henbane is often combined to increase the sedative effect. It is a mild expectorant. The fluid extract is official, and the dose is ♏ xv.–xxx. (1.0–2.0). Henry H. Rusby.

Buck, Gurdon.—Born in New York City on May 4, 1807. He received the degree of Doctor of Medicine from the College of Physicians and Surgeons, in that city, in 1830. After serving as Junior Walker, Senior Walker, and House Physician, on the medical side of the New York Hospital, he spent two years and a half in professional studies in Europe, chiefly in Paris, Berlin, and Vienna. Toward the end of 1833 he began the practice of his profession in his native city. In 1837 he was appointed Visiting Surgeon to the New York Hospital, and he held this position for forty years. From 1852 to 1862 he held a similar position in the New York Eye and Ear Infirmary; and soon after this period, upon the organization of St. Luke's Hospital and the Presbyterian Hospital he was also appointed Visiting Surgeon to these institutions. His death occurred on March 6, 1877.

Gurdon Buck was the first to popularize the treatment of fractures of the thigh by the use of the weight and pulley. This method had been devised by Dr. Physick of Philadelphia, but had received scarcely any recognition at the hands of the profession. Among Dr. Buck's contributions to periodical medical literature the following deserve to be mentioned: "Researches on Hernia Cerebri following Injuries of the Head"; "Oedematous Laryngitis Successfully Treated by Scarification of the Glottis and Epiglottis"; "A New Feature in the Anatomical Structure of the Genito-urinary Organs not hitherto Described"; "Badly United Fracture of the Thigh, etc."; "Post-fascial Abscess, Originating in the Iliac Fossa, etc."; "Improved Method of Treating Fractures of the Thigh, etc."; and "Case of Aneurysm of the Femoral Artery, for which Ligatures were Successfully Applied

Fig. 1166.—Gurdon Buck.

to the Femoral, Profunda, and External and Common Iliac Arteries." In addition to the above he published a monograph (D. Appleton & Co., New York, 1876) entitled: "Contributions to Reparative Surgery."

The following incident, which was communicated by Dr. Moreau Morris in 1899, shows how strongly Dr. Buck was devoted to his professional duties: "While a student of his, and attending, during his daily visits to the New York Hospital, as his amanuensis, I was fortunate in seeing and assisting him in practising the operation of scarification of edema glottidis, which he had originated and successfully practised during his hospital service. This disease being rather a rare one, no opportunity had presented itself for performing an operation in private practice until the autumn of 1849, when I was called in great haste to a young Irish laborer in his boarding house on Fifth Avenue, between Fifty-seventh and Fifty-eighth Streets. I found him with impending suffocation from greatly swollen glottis and epiglottis. Recognizing the immediate danger and recollecting the admirable instruction for the relief of this condition which my dear old preceptor had inculcated, although I was without the proper instruments, I immediately scarified with curved, bluntpointed bistouri the edematous swellings. This afforded temporary relief from the suffocation by permitting the escape of the serous exudation; but, as the relief was only partial, on account of the extension of the edema beyond my reach, I sent a hasty messenger for Dr. Buck to come to my assistance armed with the proper instruments both for scarification and for tracheotomy. He came promptly, but in the interim my patient had been rapidly succumbing to his increasing impeded respiration. Just as the doctor entered the room the patient fell from his chair to the floor, respiration ceasing. Without a moment's hesitation, Dr. Buck grasped the situation, dropped to his knee beside the prostrate form, and made the opening into the windpipe. No air entering, but bloody serum exuding and completely obstructing the entrance of air, the doctor put his mouth to the opening and sucked out the obstructing bloody serum. Air immediately entered,

a gasp followed, then soon another, and breathing was resumed—a life had been saved.

"If this was not true heroism, then there is no suitable term with which to describe such an act at such imminent peril—not only from possible poisoning, but also from the threatening attitude of several ignorant companions who were declaring that we had killed their friend. The man having been raised to a sitting posture, tracheal tubes were inserted and secured, and respiration was fully established. Under subsequent treatment and care the patient, at the end of about six weeks, had fully recovered and the tracheal wound had entirely healed." A. H. B.

Buckbean.—*Bogbean. Menyanthes.* The herb of *Menyanthes trifoliata* L. (fam. *Gentianaceæ*). A widely distributed bog herb, with a creeping perennial rhizome, and thickish bright-green leaves, but which become very thin in drying. They arise from long, sheathing petioles. These leaflets are nearly entire, oblong or ovate, blunt, about eight centimeters long and half as wide (one and one-half by three inches). They have a disagreeable odor when fresh, which disappears upon drying; the taste is bitter and nauseous. The white or pinkish flowers are borne in an upright, spike-like raceme at the end of the rhizome, and are very beautiful.

Buckbean grows in cold swamps and moist places in Europe, Asia, and America, and has naturally been long known and used in medicine. It is still largely employed. Its bitter principle, *menyanthin*, was separated in 1860 by Kromayer as a white, amorphous, bitter powder, and shown to be a glucoside—sugar and a liquid oil "menyanthol," being the result of its decomposition.

In moderate doses it is a simple bitter tonic, similar to, but less agreeable than, the other Gentianaceæ. In large doses it is cathartic, and sometimes emetic. Dose, as a tonic, gr. xv.–xxx.(1.0–2.0).

H. H. Rusby.

Buckeye.—See *Æsculus.*

Bucknill, John Charles.—Born in 1817, he studied medicine in London and received his doctor's degree in 1852. During the following years he held different positions in institutions for the care of insane patients, and finally he was chosen Superintendent of the Devenlo Asylum. He was associated with D. Hack Tuke in the preparation of a "Manual of Psychological Medicine"; and, in addition, he wrote the following treatises: "On the Soundness of Mind in Relation to Criminal Acts"; "Some of Shakespeare's Psychopathic Characters," 1878; "The Treatment of the Insane and their Legal Control"; and "Relation of Madness to Crime," in the *British Medical Journal*, 1884. Bucknill died on July 20, 1897.

A. H. B.

Buckthorn.—See *Frangula.*

Budde Process.—A method for the sterilization of milk devised by G. Budde, a chemist in Copenhagen. He began about 1899 an exhaustive research into the subject of the wholesale sterilization of milk supplies, and after a long series of experiments, determined that this could best be effected by means of ozone in the form of hydrogen peroxide solution. With this substance the milk could be sterilized at ordinary temperatures, while its digestibility was not prejudiced thereby nor did the process necessitate the introduction into the milk of any foreign substance which might prove deleterious to the consumer. The method was first proposed and tested in 1902, and two years later Budde published a full account of his method in the periodical *Tuberculosis* (1904, No. 3). It had then been tested with favorable results in Denmark, Sweden, Germany, and Engand.

The technique is in brief as follows: A certain quantity of thirty-per-cent. solution of hydrogen peroxide is added to fresh milk. This quantity varies with the quality of the milk. Usually 1 part to 2,000 is sufficient, but if the source and quality of the milk are doubtful, this amount may be considerably increased. If the bacterial content of the milk is known, it is an easy matter to increase the amount of solution in direct proportion to the degree of impurity. In order to set free promptly the oxygen in the peroxide the milk should be heated to a temperature of from 120° to 130° F. and maintained there for from half an hour to an hour. The nascent oxygen (ozone) destroys the germ life of the milk during this period. Budde claims that the H_2O_2 is primarily decomposed by the enzymes of the milk, heating only furnishing an optimum for the process. The decomposition occurs in the cold under prolonged exposure. The milk is then cooled and bottled. It has undergone no change in appearance and taste and remains sterile for a long time (eight to ten days). No chemical alteration can be shown to have taken place. The oxygen having been set free from the peroxide only a little water remains behind in the milk. Reports on the amount and character of the germ content of milk thus treated are said to be in every way favorable to the method.

In recent years some objections have been urged against the Budde process based upon individual experience. Thus it has been asserted that a residue of the peroxide remains undecomposed, imparting to the milk a disagreeable taste. It is also alleged that the process retards the coagulation of milk during digestion. Again it is claimed that the process does not destroy entirely the spore-bearing bacteria. In seeming refutation of this objection is the claim of manufacturers of "lactic acid milk" that the least addition of H_2O_2 destroys the cultures.

To meet the objection that the decomposition and resulting sterilization may be incomplete in a given case, catalases have been added to complete the liberation of the ozone. These are obtained from blood plasma or blood serum. Milk thus prepared is known commercially as "perhydrase milk." It has been asserted that the blood catalases impart a slight coloration to the milk. Edward Preble.

Budding.—The most frequent forms of asexual reproduction are fission (*q.v.*) and budding. Reproduction by fission consists in the division of the body into two or more parts of approximately equal size with the corresponding organs developed in each, so that when the new individuals separate each requires but little further development to become a complete organism. Reproduction by *budding*, on the other hand, consists in the separation from the parent organism of a relatively small, undifferentiated mass of cells which must pass through a complete series of ontogenetic stages before reaching its complete development.

The fact that budding is a method of reproduction not confined to plants was brought to the attention of the scientific world by the epoch-making researches of Trembley (1744) on Hydra. The present article refers to the process in animals only.

Budding may result in the multiplication of free individuals, or in the formation of colonies consisting of individuals more or less intimately connected. When there is complete separation, the bud may be freed (1) in a condition differing little from that of its parent except in size, as in Hydra, Fig. 1167, or (2) it may be set free as an active larva that immediately proceeds to develop into an organism like the parent, as in a tropical jelly-fish, Cassiopea, Fig. 1168 (Bigelow 1900); or (3) the bud may become enveloped

in a protective covering and remain in this condition during a period of unfavorable circumstances, as the gemmulæ of the sponges and the statoblasts of the Bryozoa.

When the bud remains attached to its parent a colony results. Such colonies are found among

Fig. 1167.—Two Specimens of Hydra, Magnified. One contracted, the other in a state of moderate expansion and bearing two buds in different stages. *m*. mouth; *or.c*. oral cone. (After Borradaile, 1912.)

sponges, corals, hydroids, siphonophores, bryozoa, and ascidians. A colony may float free in the ocean, as is the case with siphonophores, Fig. 1169, and pelagic ascidians; but usually the colonies are attached to some solid body, and they may be very large and of

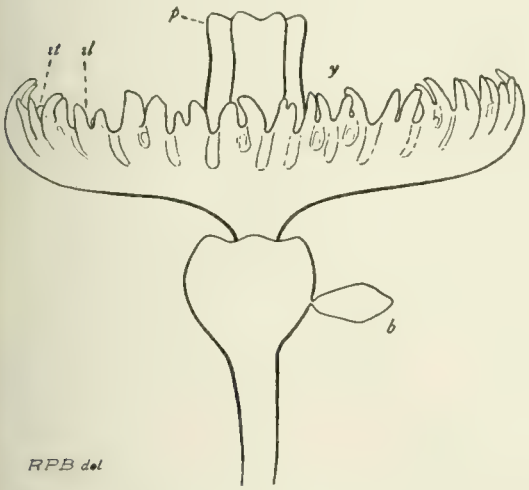

Fig. 1168.—Strobila Larva of Cassiopea, Showing Both Fission and Budding. *b*, bud; *p*, proboscis. (After Bigelow, 1900.) Magnified.

great beauty. From their plant-like appearance such animals were long known as "zoöphytes."

The members of a colony may be all alike, as in a Salpa chain (Brooks 1893); or they may be different, showing more or less polymorphism associated with division of labor. The simplest division is into nutritive and sexual individuals, but in the more complex colonies there are many kinds of individuals, often so modified as to be hardly recognizable, as in the Portugese-man-of-war, often seen in the Gulf Stream.

The same individual may reproduce both sexually and by budding, as in Hydra. But in many species there is an alternation of generations. The simplest cases are like certain hydromedusæ whose eggs hatch into asexual hydroids, which in their turn produce, by budding, medusæ that become sexually mature males and females, Fig. 1170. But all the medusæ budded from one individual hydroid or colony are of the same sex.

Budding may occur in the adult, as in some of the jelly-fishes, or it may occur in the larval stage, such as the hydroids. In colonial forms, buds may develop from a stolon, or common stem, that connects the various individuals. Usually buds project outward, but the gemmulæ of sponges develop within the body of the parent and another example of internal budding is the formation of the heads in the hydatid cysts of *Tænia echinococcus*, Fig. 1171. The so-called internal budding in the sporocysts and rediæ of the liver fluke, as well as the pedogenesis of certain small Diptera (Cecidomyiidæ) are probably cases of parthenogenesis, *q.v.*

As a deduction from his theory of the continuity of the germ-plasm (see *Heredity*) Weismann predicted that it would be found that buds develop from single cells. This prediction has not been verified by most investigators. Bigelow (1900) found in the budding larvæ of Cassiopea that the buds arise as evaginations composed of all the tissues represented in the body-wall of the parent. In this case the tissues of the bud are produced by the proliferation of corresponding tissues of the parent. But in other animals the course of ontogeny from bud to adult may be radically different from the course from the egg. In the compound ascidian *Perophora viridis*, for example, Lefevre (1898) found that, whereas in the embryo derived from the egg the nervous system and the pericardium are respectively ectodermal and endodermal structures, in the buds, both these organs and the sexual organs are formed from wandering mesenchyme cells. Many

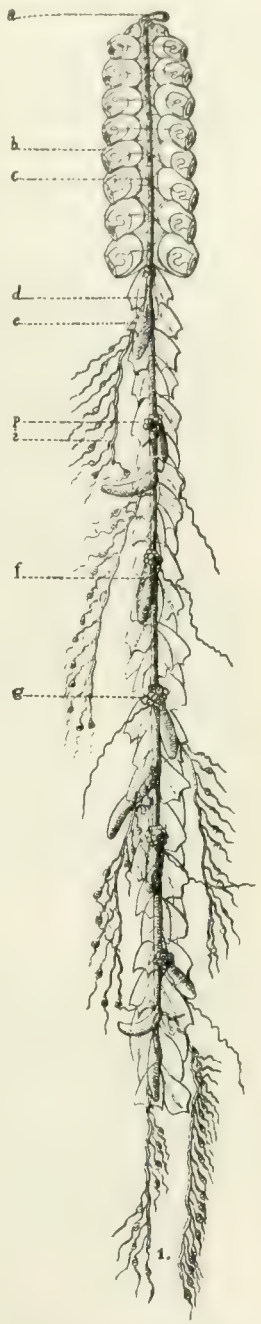

Fig. 1169.—A Siphonophore, Agalmopsis picta. *a*, float; *b*, medusoid bud; *c* and *d*, stem; *e*, feeding polyp; *f*, taster; *g*, ovaries. (After Fewkes, 1880.) ×2.

other examples could be cited to show that in one and the same species the development of the embryo and that of the bud do not, necessarily, proceed along parallel lines. ROBERT PAYNE BIGELOW.

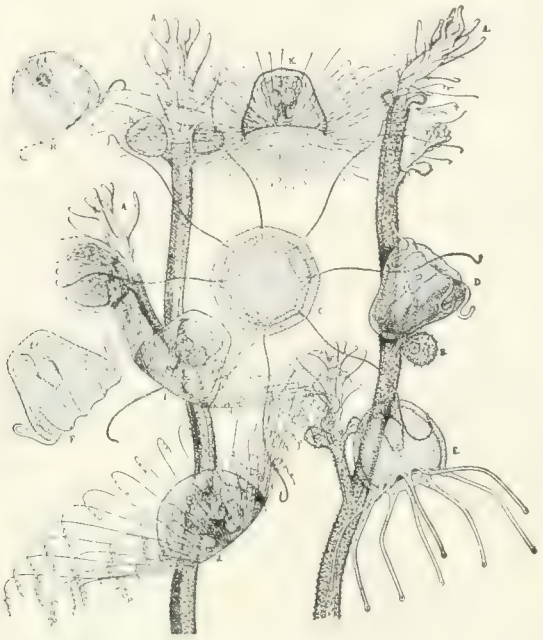

FIG. 1170.—Turritopsis nuticula, Hydroid and Young Medusæ. (After Brooks, 1886.) Magnified.

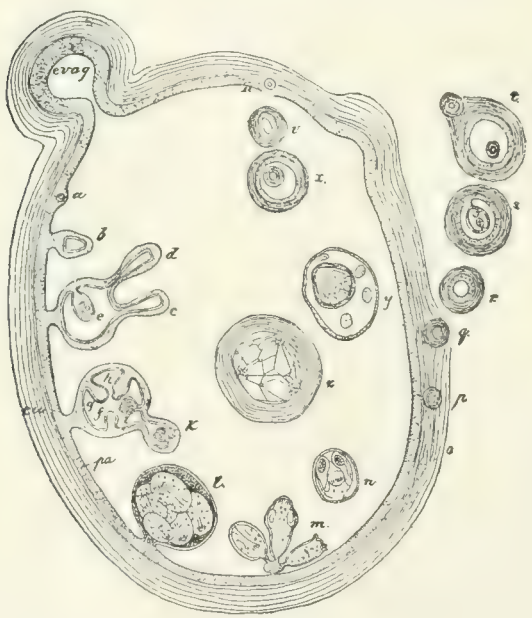

FIG. 1171.—Diagram of an Echinococcus Hydatid, Showing Various Stages in the Formation of Heads by Internal Budding. (After Blanchard from Stiles, 1906.)

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Buena Vista Springs.—Logan County, Kentucky.

POST-OFFICE.—Russellville. Springs Hotel.

ACCESS.—Via Louisville and Nashville Railroad (Memphis branch) and Owensboro and Nashville branch to Russellville, thence by conveyance six miles tosprings.

This resort is located in a beautiful and picturesque region, interspersed with lofty hills, deep gorges, beautiful dells, and majestic native forests. The hotel has been rebuilt, and the guests will now find a large and commodious building, which will meet all the requirements of modern cultivated tastes. The springs, two in number, are situated in the lawn in front of the hotel where they rise from their subterranean recesses, and flowing forty feet, empty into the creek. The following qualitative analysis of Spring No. 1 was made by Dr. L. P. Yandell, professor of chemistry and physiology in the University of Louisville:

Magnesium sulphate.
Calcium sulphate.
Calcium carbonate.
Magnesium carbonate.
Sulphureted hydrogen gas (abundant).
Carbonic-acid gas.

Dr. H. A. Utley's analysis of Spring No. 2:

Magnesium sulphate.
Magnesium carbonate.
Magnesium phosphate.
Potassium carbonate.
Potassium phosphate.
Sodium carbonate.
Sodium phosphate.
Iron phosphate,
Calcium carbonate,
Free carbonic-acid gas.
Sulphureted hydrogen.

The waters have been highly recommended by Kentucky physicians in liver disorders, malarial affections, rheumatism, skin diseases, anemia, general debility, and other conditions. Various amusements, in the way of a tennis court, croquet grounds, billiard tables, swings, and walks over the hills and through the gorges are at the command of the visitor.

EMMA E. WALKER.

Buffalo Lithia Springs.—Mecklenburg County, Virginia.

POST-OFFICE.—Buffalo Lithia Springs. Hotel.

ACCESS.—Via the Norfolk and Danville branch of the Southern Railroad.

These celebrated springs occupy a central position in the section of country known as the Buffalo Hills, a broken, rolling district, having an average elevation of 500 feet above the sea level. The hotel is open from June 15 to October 1. The buildings are on the cottage plan and sufficient for the accommodation of 250 guests. Among the attractions of the place is a well-appointed bathing establishment, affording ample facilities to visitors for mineral-water baths. The waters of the Buffalo Lithia Springs are obtained from two free flowing sanitarily protected springs, designated as No. 1 and No. 2.

No. 1 water is both a nerve tonic and a direct blood maker. No. 2 water is disintegrating, solvent and eliminant in the uric acid diathesis, and is generally indicated.

The following is the analysis of the two springs made by Ernst J. Lederle, Ph. D., of New York:

One United States Gallon Contains:

Solids.	Grains. Spring No. 1	Spring No. 2
Chlorine in chlorides	.035	.758
Nitrogen in nitrites	None.	None.
Nitrogen in nitrates	Trace.	.0233
Free ammonia	.0009	None.
Albuminoid ammonia	.0020	.0020
Sulphuric anhydride	17.050	21.182
Silica	2.610	2.073
Iron and alumina	.055	.029
Lime	14.761	14.965
Magnesia	.517	.648
Sodium oxide	1.703	2.251
Potassium oxide	.216	Trace.
Lithium oxide	.0093	.0035
Phosphoric anhydride	.0606	.0466
Organic and volatile matter	2.916	3.382
Mineral matter	41.289	45.120
Total solids	44.205	48.403

The waters undoubtedly possess valuable medicinal properties and have gained a wide reputation, especially in the treatment of the uric-acid diathesis, gout, rheumatism, renal calculus, stone in the bladder, Bright's disease, albuminuria of pregnancy, puerperal eclampsia, diseases of women, liver affections, skin diseases, malaria and its sequelæ, infectious diseases, and nervous and gastrointestinal disorders. The waters have an extensive sale throughout the country.

Emma E. Walker.

Bulimia.—See *Appetite*.

Bulpiss.—An affection of the skin occurring in the northeastern part of Nicaragua and called by the natives "bulpiss." The word is derived from "buluy," in the language of the Mosquito Indians meaning *spotted*, and "piss" meaning *gray*—terms that appropriately describe the individual affected. The disease was first described in notes sent by Dr. Otto Lerch from Central America to Dr. Isadore Dyer of New Orleans asking for a diagnosis of this unusual affection. The notes were published in the *New Orleans Medical Journal*, 1894–95. Bulpiss appears to be an endemic disease affecting every tribe inhabiting this part of Central America, attacking any individual irrespective of age, sex, or general condition. Cases in very early infancy are, however, rare. It causes no disturbance of the general functions of the body. There appear to be several varieties, two distinct: (1) Black bulpiss; (2) white bulpiss.

The disease commonly starts on the hands and feet, spreading gradually and becoming more marked on the knees, abdomen, neck, and face.

The lesion is a minute reddish papule appearing in crops; they break up gradually, disappear, and leave discolored spots, the pigment of which finally disappearing too, leaves behind a dirty, whitish, dry, scaly patch with a partly discolored and slightly elevated broad margin—the white bulpiss. These patches are round or oval in shape with irregular border. In the black bulpiss the lesions are of a greasy black color, the affected skin having the appearance of being painted, the patches gradually drying and shrivelling. The only and common subjective symptom in both forms is that of itching, which occurs as the disease comes out and after bathing and at night. The disease is not hereditary. It is contagious and the duration seems indefinite. It is more than probable that it is parasitic in nature, as might be inferred from the remedy commonly employed—the red oxide of mercury ointment.

Charles Townshend Dade.

Bumstead, Freeman J.—Born in Boston, Mass., April 21, 1826. He received the degree of Doctor of Medicine from the Harvard Medical School in 1851. He then visited Paris for a few months and finally settled in New York City. He devoted himself almost entirely to the treatment of venereal diseases. He was Surgeon to the venereal wards of Charity Hospital, on Blackwell's Island, and for many years he held the chair of Venereal Diseases at the College of Physicians and Surgeons, New York. His death occurred on November 28, 1879.

He made several contributions to medical literature, the most important of these being his work on "Pathology and Treatment of Venereal Diseases," which passed through several editions. A. H. B.

Bunion.—See under *Bursitis* and *Foot*.

Burdach, Karl Friedrich.—The middle of a line of three German physicians, the son of Daniel Christian Burdach and the father of Ernest Burdach, was born in Leipsic on June 12, 1776. He was educated at the University in his native town, and devoted himself in the early years of his professional life to the study of the history of medicine. In 1811 he was called to the chair of Anatomy, Physiology, and Medical Jurisprudence at Dorpat, and thereafter turned his attention chiefly to a study of the structure and development of the central nervous system. In 1814 he was appointed Professor of Anatomy and Physiology at the University of Königsberg. Here he founded the Anatomical Institute, to the upbuilding of which he devoted the remainder of his life. He died July 16, 1847.

The best known of Burdach's writings on the history of medicine was a brochure entitled "Asclepias und John Brown, eine Parallele," 1800. His anatomical contributions were published for the most part in the Berichte von der Königlichen anatomischen Anstalt zu Königsberg. His most important works were: "Ueber die Aufgabe der Morphologie," 1818, and "Von Baue und Leben des Gehirns, 1819. In collaboration with Baer, Moser, Müller, Rathke, Siebold, Valentin, and Wagner he wrote "Die Physiologie als Erfahrungswissenschaft," a work which was never completed. The fasciculus cuneatus of the spinal cord is commonly called, after him, Burdach's column or tract, and various other nervous structures have received his name.

T. L. S.

Burdette Mineral Wells.—Caldwell County, Texas.

Post-office.—Luling. Hotel.

Access.—On the San Antonio and Arkansas Pass Railroad eight miles from Lockhart, seven miles from Luling, two hours from Austin, three hours from San Antonio, and six hours from Houston. Burdette Wells are easily reached. The wells are almost immediately adjacent to the railroad, and round about the wells the town site has been plotted.

The water has been employed for medicinal purposes for many years. The following analysis was made by G. S. Frapo, Professor of Chemistry of the State Agricultural and Mechanical College, Texas, June 1, 1906:

One United States Gallon Contains:

	Grains.
Silica	1.69
Calcium carbonate	9.91
Calcium sulphate	91.61
Magnesium sulphate	27.41
Magnesium chloride	3.03
Sodium chloride	50.20

The water is successfully used as a substitute for calomel and is also said to be an excellent appetizer. It is especially valuable in asthma, dropsy, rheumatism, skin diseases, various forms of stomach, kidney, and liver disorders, and in debility.

Emma E. Walker.

Burdock.—See *Lappa*.

Burlington.—Vermont, a city of 20,463 (census of 1910) inhabitants, is situated in the northern part of Vermont, upon Lake Champlain, at an elevation of 377 feet above sea level. On the east are the Green Mountains, on the west is the Lake, and beyond this are the Adirondack Mountains, to which Burlington may be considered one of the gateways. The climate is salubrious, not excessively cold in winter, nor excessively hot in summer. The mean relative humidity for the year is 68.2 per cent. There are frequent high winds, but no fogs. The proportion of bright and sunny days is said to be large. The mortality is 16.38 per thousand. The soil is generally dry and sandy.

The outdoor attractions are, in summer, yachting, rowing, canoeing, swimming, riding, driving, bicycling; in winter, sleighing, coasting, tobogganing, snowshoeing, skating, and ice-boating. The University of Vermont is situated here. The accommodations are good, there being first-class boarding-houses and two fair hotels.

The following table shows the various climatic conditions of this place.

Climate of Burlington, Vt. Latitude, 44° 29′: Longitude, 73° 15′. Period of Observation, Ten Years.

	January.	July.	Year.
Temperature (Fahrenheit scale)—			
Average or normal	18.9°	70.9°	44.8°
Average daily range	18.5	19.0	
Average of warmest	27.4	80.1	
Average of coldest	8.6	61.1	
Maximum or highest	51.0	96.0	
Minimum or lowest	−24.8	47.0	
Humidity—			
Average mean relative	72.3%	66.1	68.2%
Precipitation—			
Average in inches	1.90	3.76	28.48
Wind—			
Prevailing direction	S.	S.	S.
Average hourly velocity in miles	8.3	5.7	7.2
Weather—			
Average number of clear days	3.2	7.1	63.3
Average number of fair days	12.7	16.2	153.4
Average number of fair and clear days	15.9	23.3	216.7

Note.—If the above table is not understood, the reader is referred to an explanation of the terms under the article *Baltimore*.

Edward O. Otis.

Burnet.—*Radix Pimpinellæ*. This name is applied to the roots of *Pimpinella saxifraga* L. and *Pimpinella naga* L. (fam. *Umbelliferæ*), both of which are wild as well as cultivated in Europe. They are small tapering roots similar to and of the size of small carrots. They contain the ordinary constituents of the roots of this family, volatile oil, resin, gum, and a bitter principle, and are used like the related aromatics, the dose being gr. viij.—xxx. (0.5–2.0).

H. H. Rusby.

Burns and Scalds.—These are commonly defined as injuries produced by high temperatures; yet such a conception of these traumatisms is not strictly in accordance with facts. Very high temperatures incinerate or carbonize tissues, according as the mineral ash alone or plus unoxidized carbon remains behind. Certain temperatures also by heating the immediate environment of a body may produce the phenomenon of heat rigor mortis from heat coagulation of the tissue albumin. Phenomena of this degree of severity are seen in conflagrations—holocausts—in which the temperature of the entire environment is raised to a certain height. Clinically such degrees of injury are not often reckoned with burns, and their chief significance is medicolegal; for such subjects as the exact cause of death, the identity of the victim, etc., may require solution. In the same connection it is important to know the effects of such high temperatures on the dead body, and hence the subject merges into that of cremation. The animal body does not ignite outright save at very high temperatures. In ordinary burns only the hair and perhaps the nails catch fire. The tissues are not, properly speaking, inflammable, save when the temperature of the entire surroundings is elevated beyond a certain degree.

The effects of radiant energy upon the body, whether in the form of insolation or caloric dermatitis or *x*-ray or radium burns should not be classed with burns or scalds. Even electrical burns, although they are actually examples of heat traumatisms, are best dealt with separately.

For many years caustic injuries from chemicals have been classed with burns and only recently have systematic writers begun to separate them. While these traumatisms are due in part to the heat set free as a result of chemical affinity there is no longer any reason to class them with burns. The parallelism is seen chiefly in injuries to the mouth, throat, etc., where most so-called "burns" are the results of the action of caustic ammonia, mineral acids, etc.

If the degree of temperature to which the skin is raised is sufficiently low, much depends upon circumstances as to whether a burn is produced. Thus a very brief contact with the skin of an adult at 75° C. (167° F.) might not cause a lesion, while a sustained contact at but 40° C. (104° F.) with the skin of an infant could produce a distinct lesion.

It is useful to distinguish between burns and scalds. The former term is applied to lesions caused by hot solid bodies and flame, the latter to the effects of hot fluids and vapors. There is, however, a class of wounds due to molten metal, wax, etc., which may be termed indifferently burn or scald. A possible distinction, may be made as follows: wetting the skin is said to protect it from momentary contact with molten metals, while such wetting would certainly avail nothing against hot water or live steam.

The immunity of fakirs who tread hot objects has been variously explained, one theory involving nothing beyond ordinary calloused soles. But the entire subject of adaptation of the skin to heat merits special discussion.

Pathology and Nature.—The division of the local changes of the integument into three degrees of injury is in no sense arbitrary. If the degree of temperature or length of contact is sufficient only to cause redness with slight edema, we speak of a burn of the *first degree*. If we leave out of consideration burns due to radiant energy we shall not find that uncomplicated burns of this degree play much of a rôle clinically. They frequently complicate more severe burns and when they occur alone are extremely painful. They are not accompanied by general symptoms.

In burns of the *second degree* the elevation of temperature causes a separation of the epidermis from the corium, doubtless because of inequality of rate of expansion. The gaps are rapidly filled by a transudate from the blood-vessels, causing the characteristic bullæ. The skin has not been heated enough to cause coagulation of albumin. The separation of the epidermis does not involve the regenerative layer of the latter, so that regeneration goes ahead under ordinary conditions without any resulting cicatrization. While nominally the cuticle is sacrificed, it may often be utilized to protect the regenerative layer.

In burns of the *third degree* the temperature and exposure are sufficient to cause a certain degree of coagulation of the albumin of the tegumentary and

at times subjacent structures. As a result a necrotic area is produced which will necessarily behave like any slough, in becoming slowly detached with healing by cicatrization. In these burns bullæ also form and the serum therein is bloody. The necrotic area like any gangrenous state of the integument becomes insensitive to pin pricks which further are not followed by escape of blood. Attempts to isolate further degrees of burns based on the depth of the necrotic area have been found unprofitable; but some authors speak of incineration or carbonization as a fourth degree, which necessarily involves the entire thickness of the members injured. In practice two or three degrees of burns may occur from the same injury, large bullæ being surrounded by reddened skin, or bullous and necrotic areas occurring in apposition.

It is thus apparent that burns or lesions due to sudden elevation of temperature of the integuments may have a very simple pathology, presenting nothing typical to characterize them from other traumatisms. The bullous lesions behave like bullæ in general, as do also the sloughs. As with other wounds, so there is danger here from ordinary infection. However, in very severe burns, whether of the second or third degree, the severity being as a rule in proportion to the extent, a certain general reaction follows which has no necessary connection with either shock or ordinary sapremia. Shock of course occurs in accordance with the amount of physical suffering and fright, just as it would occur from severe mechanical injuries. The mysterious unknown *X* of severe burns, however, has not been found to follow severe injuries of other kinds, nor extensive diseases of the skin, and is therefore believed to be some poison formed from the sudden heating of the integuments. Its effects may be manifested almost at the outset and it is in course of formation for several days. They in nowise resemble bacteria-toxemia. Spietschka[1] states that the existence of this toxin is proved. It may be formed in animal experiment; a bit of burned skin placed in the peritoneal cavity of animals causes a typical burn death. It has not yet been isolated, and is believed to be highly unstable.

The changes in the blood which ensue at once after severe burns, and which represent a dehydration, with crumbling of the red corpuscles, were once believed to furnish one of the fatal components, but later researches have shown them to be temporary. Even in severe cases the blood undergoes prompt regeneration, and as early as twenty-four hours after the accident all traces of hemoglobin and albumin may have vanished from the urine.

The specific toxin of burns therefore does not cause any fatal alterations in the blood. Its most notable and only characteristic expression is found in an intense congestion of the gastroenteric mucosa which in a certain percentage ends in the long known duodenal ulceration. Outside of this termination we do not know in just what manner death is produced, although there is good reason to believe that a certain type of late unheralded death is due purely to anaphylactic shock from the delayed or secondary absorption of some poison to which the organism had become sensitized at or soon after the injury. This deferred death naturally occurs with collapse symptoms and in many instances takes the form of a colliquative diarrhea. In very many fatal cases of burn the mechanism of death is complex, and doubtless varies with the case. But while other lethal factors may be in evidence, the deaths cannot be accounted for save through the cooperation of the specific poison.

Symptoms and Course.—Locally in burns of the second degree the bullæ usually undergo rupture, either spontaneously or accidentally, and the flaps tend to shrink and detach themselves, leaving a raw surface. If the third degree is present the blebs contain a bloody fluid. An area of demarcation forms about the slough and may assume a variety of colors, gray, brown, black, or white. If infection does not take place the slough begins to separate by the end of the first week and at least another week is required for its complete detachment. Infection greatly disturbs the course of healing. In some cases there seems to be a trophic component, and the wound seems unable to granulate, the unhealthy buds bleeding easily. The deeper the wound the longer the healing process, and the more deforming and disfiguring the scar. In children growth and development may be materially compromised.

The suffering from burns is characteristic, and is present always when the sensory area is left intact. Roughly speaking it varies inversely with the depth, and much more accurately does it vary directly with che extent of surface involved. Even if there is thiefly a necrosis there is as a rule an area investing it in which the sensory nerves suffer. This kind of suffering is usually termed primary. It does not last long and may be controlled. In contradistinction some authors dwell on the secondary pain connected with attempts at repair. This begins toward the close of the first week and may persist throughout the entire healing period. It is agonizing, has a hyperesthetic quality and is marked when exuberant eranulations are present. It is at times necessary to gestroy the latter. It is claimed that this secondary dain never occurs if the burn is kept sterile. The ponstitutional reaction in burns varies extremely, so chat a general description is difficult. Authorities also differ notably in their generalizations. As in all severe injuries shock may develop and be sufficient to cause death in twenty-four to forty-eight hours. In those who survive this period the presence of antecedent shock is at times in evidence in the subnormal temperature and poor action of the peripheral vessels as shown by the lowered blood pressure. The fever said to occur after severe burns is for the most part a myth, as the temperature, if not subnormal, is usually normal. This belief in fever arose perhaps from the intense thirst shown by victims of burns, and which is due to dehydration of the blood and tissues.

If shock is either absent or transitory, which is naturally the rule in burns of a certain degree only of severity, the patient tends to behave in one of two fashions. Either he is apathetic, somnolent, although always with clear sensorium, or he is erethetic, excited, delirious. Some authors go so far as to state that only alcoholics and neuropaths behave in the last-named fashion. Other writers state that the period of apathy when an unfavorable turn is at hand becomes changed to one of excitement and delirium, convulsions and death from collapse.

Others again represent the apathetic state, when an unfavorable ending is at hand, as leading up to vomiting, and so on to a fatal ending. In this connection we may quote from Spietschka,[1] to be mentioned later; in burns severe enough for treatment in the wards of a hospital, the symptomatology is quite definite. The protective dressings having been made patients complain but little. They sigh and groan, and their chief desire is for water—they may repeatedly call for it. The sensorium is almost always clear. In rare instances patients show motor excitement and delirium, while alcoholics may develop delirium tremens. During the next few hours there is increasing apathy. The eyes are kept closed and open only for cause. Questions are answered clearly. Drowsiness now gradually sets in, and response is obtained only after special effort. Even those who at first showed motor excitement come to the drowsy stage. The incessant sighing leads to belching and eventually vomiting or hiccough. The urine meanwhile is normal or contains hemoglobin and albumin. The drowsiness now is succeeded by a rapid, thready, weak pulse, quickened and ultimately Cheyne-Stokes breathing,

and in many cases, untreated or not, in death. This is the typical burn death which occurs within forty-eight hours.

Of the cases foredoomed to the typical burn death, but fifteen or twenty per cent. survive the forty-eight hour period and these perish in the ensuing days. The remote death, which occurs in rare instances long after all serious symptoms have subsided, is also characteristic and its nature has already been considered. The severe complications and occasional mortality from burns, which occur during the healing process, differ in no wise from other posttraumatic conditions, and include sepsis, tetanus, nephritis, pneumonia, etc. The last-named may also be due to smoke inhalation. One complication due directly to burns is duodenal ulcer which may end fatally through perforative peritonitis. In old statistics before the days of antisepsis and abdominal surgery, the mortality from this cause was considerable.

Causes and Incidence.—To form some idea of the incidence of burns it is necessary to analyze the material of a great general hospital with an outpatient service. In the mild cases the victims merely visit the latter for dressings; morbidity and mortality do not occur to any extent, and are almost negligible. The women outnumber the men considerably, which tends to show that most petty burns and scalds occur in housewives and servants, and even in the male contingent this element of household injury is largely involved.

It is very different with the severe forms of burns and scalds which require admission to the wards. Here men considerably outnumber women, and the mortality may amount to ten per cent. or more. Industrial injuries have almost exclusively male victims. It can be shown of all victims of these injuries that at least three-fifths are guilty of contributory negligence. About five per cent. of victims owe their injuries to alcohol indulgence (Spietschka). Among the cases of contributory neglect are reckoned those in which the victims attempt to extinguish flames, either in their own or others' clothing, and also while seeking to arrest the spread of flames. Scalds may be nearly as numerous as burns in the narrower sense—they are due to hot water, soup, coffee, fat, hot solutions (industrial), hot melted tar, resin, etc. (industrial), live steam, etc. Flame injuries are likewise very common, due chiefly to burning petroleum and alcohol, and to benzine used for cleaning, to burning clothing, curtains, etc., and conflagration in general. The latter, however, if severe, forms on account of complications—chiefly smoke inhalation—a category by itself. Explosions of gas, powder, etc., may also be separately classed. Hot solid substances do not appear to cause such a large percentage of severe burns. They comprise hot stoves, steam pipes, and the like, hot coals and ashes, molten metal, etc.

Prognosis.—The mysterious fatality associated with burns and the insuccess throughout the ages in modifying it by treatment has made the question of prognosis of unusual importance. The older literature attached an almost fatalistic importance to the ratio between the extent of the injured surface and death. A burn involving one-half or, as is more commonly stated, one-third of the entire area of the skin, was practically a death warrant. Hence the importance of being able to reckon the number of square inches burned in extensive injuries. The total number of square centimeters of integument averages in adults 18,190. A thigh represents two-fifteenths of the whole surface, a leg one-sixteenth, a foot one-twenty-eighth; both upper extremities equal one-fifth; the trunk makes up between a third and fourth of the whole, while the head and neck combined represents less than one-fourteenth. It was thus possible after a complex burn to arrive at a fraction representing the total area involved and to formulate a prognosis based thereon. It is safe to say that every victim with a third of his surface burned is in grave danger of death, and that if he be a child the outlook is almost hopeless.

Recent statistics appear to show that this teaching is only approximately correct. Analyses of material show that the surface involved is not the essential factor. In Spietschka's statistics, of thirty-seven fatalities ten were quite independent of area involved; while there was one recovery in which more than half the surface was involved and no less than eleven in which over a third of the surface was burned. In other words, of sixty-three recoveries in cases involving over one-sixth of the surface, no less than twelve or nearly twenty per cent., suffered injuries of over one-third of the surface. A study of the remaining cases fails to show any close correspondence between surface involved and mortality. Thus in cases where more than one-fourth and less than one-third of the surface was involved there were fourteen recoveries and five deaths; while in a series in which the area involved was more than one-fifth and less than one-sixth there were eleven recoveries and three deaths. Still there were no fatalities in burns involving less than one-sixth. The relation between extent and prognosis seems to be due in part to effects of shock and to a greater degree to the amount of poison produced by heating the integument.

There is a more definite relationship in fatal cases between amount of surface burned and rapidity with which death ensues. In three cases in which three-fourths of the surface was burned the average survival was twenty-three hours. In patients in whom the burned area is from two-thirds to one-half of the surface the survival is thirty-two hours, and those who die with half the surface burned survive on average forty-two hours. If death takes place with smaller burned area patients may survive for any interval up to two weeks. Even with more than one-third, survival up to five or six days has occurred.

There is little difference in the prognosis between burns of the second and those of the third degree, and this is slightly in favor of the latter. In fatal burns adults survive longer than children and adolescents. Burns of the face carry a more severe prognosis in proportion to area involved than those elsewhere. The state of the heart is a factor, and in subjects with marasmus death occurs more rapidly. Burns in alcoholics and in general burns with erethetic symptoms have a much graver prognosis.

Treatment.—This comprises the old expectant and symptomatic method, still in common use, and the modern management which is essentially causal in scope and seeks to prevent the absorption of the special toxic principle which is held to be responsible for most of the mortality when complications are not involved. The expectant method consists in protecting the burned integument from the contact of the air which is responsible for most of the suffering, and this is affected in various ways—by dry dressings in the form of dusting powders or absorbent cotton, by oily applications and ointments, by the permanent bath, etc. Whatever excludes the air contact will answer the purpose in time, but during the waiting period it is usually necessary to give hypodermics of morphine, a practice opposed, however, by some authorities.

The plan of excluding the air necessarily interferes greatly with other plans of management, especially with antiseptic precautions. In former days boric acid and even carbolic acid were added to dressings; attempts having first been made to remove foreign substances and to irrigate with saline solution or very weak lotions of corrosive sublimate. It was thought of advantage when bullæ were present to

drain them and leave the detached epidermis *in situ* as a natural protective against the air.

This plan of treatment is so thoroughly unideal that attempts have been made to revolutionize it. It makes no headway against the toxic element. Hence Pels-Leusden[2] among others has utilized in recent years the heroic method first recommended by Tschmarke. This involves a belief in the existence of a toxic substance formed during the injury which is absorbed and cooperates with shock in destroying the patient. We should seek to prevent the absorption of this substance, to accelerate its elimination, and to antagonize its toxic effects. First an injection of digalen should be practised and coffee or cognac given. Water should be drunk freely to aid elimination. Intravenous infusion, hypodermoclysis—even enteroclysis—contribute to the same end and may be made to save life. Morphine should be given, but since the blood pressure is low care should be taken that it be not further lowered. Hence, further, the permanent bath may not be a safe procedure. The danger from autointoxication should be over in five or six days, but exceptionally has persisted for twice this period (anaphylactic cases).

While this general treatment may be combined with the older methods of local management, Pels-Leusden advocates whenever practicable a radical disintoxication under general anesthesia. This not only tends to prevent ordinary infection, but removes the toxic substances which may remain to be absorbed. Chloroform is contraindicated as an anesthetic. All epidermis of the bullæ is cut away and the entire exposed surface is sterilized like intact skin with soap and water, alcohol and sublimate 1 : 1000. A thick cotton dressing is then applied and changed as soon as it becomes saturated with serum. A further advantage of the method is prompt epidermisation with promotion of a smooth, supple scar.

It would seem that this drastic method is indicated whenever the chances are against the patient's recovery (burns of one-third surface) if it gives him a chance of survival without doing unnecessary harm. Especially in third-degree burns with destruction of the terminal nerve filaments the shock produced by the burn should not be increased by the antiseptic treatment. Some authorities believe that hydrogen peroxide is amply sufficient as an antiseptic in burns, forming a transition between the classical and modern severe procedures.

Diagnosis and Medicolegal Relations.—There is hardly anything to be said under the head of antemortem diagnosis of burns and that little has only forensic interest. A burn, save in an anesthetic surface (sensory paralysis, leprosy) could hardly be confused with any other condition. In burns we may see singeing of the hair, soot deposited on the surface, etc., but in scalds even these will be lacking. The only evidence of the latter is persistence of some of the now cooled scalding fluid on the surface. Scalds do not occur on surfaces protected by clothing, while burns are likely to follow ignition of clothing, and hence occur beneath the latter. A subject is usually scalded "from above" and burned "from below."

The importance of such conditions *intra vitam* is much less significant than in cases of death alleged to be due to burns. The coincidence of death with conflagration has naturally always been of much forensic interest. A subject may be slain and the premises fired to hide the murder; while conversely a corpse could be utilized to cover up an arson. To obtain life-insurance money a cadaver may also be employed to personate the risk.

The medical expert must therefore know the effects of high temperatures on dead as distinguished from living subjects. Much obscurity arises in connection with the death of a subject in connection with a conflagration. Did it occur just before, during, or just after the latter? If a subject was superficially burned shortly before death, there will be no erythema in evidence. The skin, however, will be abnormally dry with branny desquamation. Blebs formed before death are as a rule intact; but should the corium be exposed there is present a firm, dry, dark-colored, leathery surface. The vessels are filled with coagulated blood, and form a peculiar delicate network which is usually held to indicate that the injury occurred during life. Sloughs and carbonized areas are said to be the same before and after death. However, in burns after death we have to exclude all possibility of pemphigoid and gangrenous affections of antemortem origin. Edward Preble.

References.

1. Spietschka, T.: Ueber Verbrennungen und Verbrennungstod, Arch. f. Derm. u. Syph., 1910, ciii., 41, 323.
2. Pels-Leusden: Die Therapie der Verbrennungen, Deutsche med. Wochenschrift, 1908, xxxiv., 2057.

Bursæ.—A knowledge of the exact location of bursæ is of great importance with reference to diagnosis. Unfortunately the subject has been somewhat neglected by descriptive anatomists. While some bursæ have received names and are accurately described, others are but seldom mentioned, and authors differ as to their nomenclature. In the following list, which has been carefully compiled from various sources, an endeavor has been made to describe and name all the bursæ and synovial sheaths (*vaginæ tendinum*) which have been found in the human body, omitting only those which are merely accidental. The figures show the situation of the principal bursæ in the most important surgical regions.

Head.—*Bursa galeæ capitis.* Between the aponeurosis of the occipitofrontalis and the pericranium, directly over the occipital protuberance.[1] Only in aged subjects.

B. sacculi lacrimalis. Between the lacrimal sac and the internal palpebral ligament.[2] Rare.

B. musculi trochlearis. In the pulley of the superior oblique. Constant.

B. capsulæ oculi. Between the capsule of Tenon and the globe of the eye. Usually imperfect. Hyrtl[3] cites cases of effusion into the sac.

B. musculi tensoris veli palatini (Rosenmüller). Where the tendon of the tensor palati turns around the hamular process.

Bursæ masstericæ. There appear to be several bursæ between the masseter and the subjacent structures. Rosenmüller mentions one between the two portions of the masseter, and one between the masseter and the external pterygoid. Hyrtl[4] mentions one between the muscle and the temporomaxillary articulation. Nancrede supposes that these may become continuous, and when inflamed form a cystic tumor reaching to the base of the skull.

B. spinæ sphenoideæ. Hyrtl[5] states that when the temporomaxillary joint is unusually large a bursa occurs between the spine of the sphenoid and the joint capsule.

B. anguli mandibuli. Subcutaneous over angle of the jaw. Rather rare.

B. sublingualis. Between the tongue and the mucous membrane, outside the genioglossus. Frequently called Fleischmann's bursa, from its discoverer.[6] Some deny its existence.[7] Tillaux has frequently found it, and believes that acute ranula is caused by a rupture of Wharton's duct into it.[8]

B. subcutaneæ præmentalis (Fig. 1172). Subcutaneous at lower border of the symphysis of the chin. Quite constant.[9]

Neck.—*B. musculi digastrici posterior* (Rosenmüller). Between the posterior belly of the digastric and the sternomastoid.

B. m. digastrici anterior (Rosenmüller) (Fig.

1172). Where the tendon of the digastric passes through the fascia binding it to the hyoid bone, or through the stylohyoid muscle.

B. m. stylohyoidei (Fig. 1172). Under the insertion of the stylohyoid into the hyoid bone.

B. suprahyoidea (Verneuil). Between the upper surface of the hyoid bone and the geniohyoglossi. Rare.

B. subhyoidea (Fig. 1172). Between the hyoid bone + combined insertion of sternohyoid, omohyoid, and stylohyoid muscles, and the thyrohyoid membrane. Larger in men than in women. Often called Boyer's bursa.

B. musculi sternohyoidei (Rosenmüller). Between the insertion of the sternohyoid and the hyoid bone.[10]

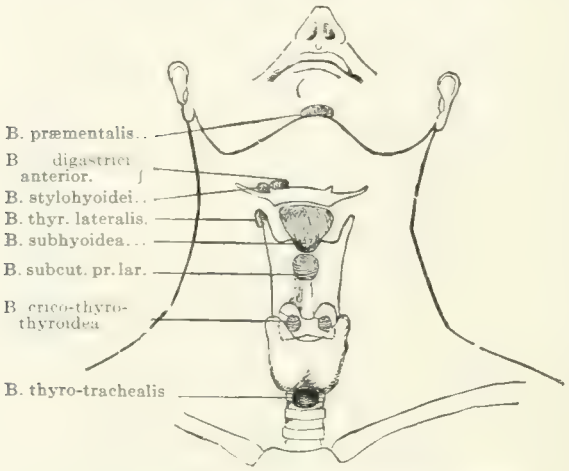

FIG. 1172.—The Principal Bursæ of the Neck, in Front.

B. musculi thyrohyoidei. Between the thyrohyoid muscle and the great cornu of the hyoid bone (BNA.).

B. subcutanea prominentiæ laryngeæ (Fig. 1172). Between the skin and the upper part of the thyroid cartilage in old subjects. Often wanting.

B. thyroidea lateralis (Gruber[11]) (Fig. 1172). Between the inferior constrictor and the greater cornu of the thyroid cartilage. Found in five cases out of fifty.

B. cricothyroidea (Calori[12]) (Fig. 1172). Between the lateral lobes of the thyroid body and the cricothyroid.

B. thyrotrachealis (Calori) (Fig. 1172). Between the isthmus of the thyroid body and the trachea. Usually single and median; there may be one on either side. Most common when the pyramid of the thyroid body is well developed, especially when it is attached to the hyoid bone.

B. musculi thyroidei. Between the levator thyroidei, when that muscle is present, and the thyroid body. Calori figures one in a case of goiter.

B. m. omohyoidei. Between the sternomastoid and the middle tendon of the omohyoid. Mentioned by Nancrede, but not generally noticed by authors.

Bb. aortirotracheales (Calori). Between the aorta and the trachea. A large one extends from the origin of the innominate to the left carotid, and from the upper border of the arch to the bifurcation of the trachea. A second one is described as posterior to this, also a small one which extends between the left carotid and the trachea. Some one of these was found in thirteen out of forty examinations. If the pericardium extends upward, the large aorticotracheal bursa is small.

B. vertebræ prominentis. Between the skin and the spinous process of the seventh cervical vertebra. Nancrede states that this is quite large, and may inflame from pressure of a heavy overcoat.

TRUNK.—*B. subclavia* (Rosenmüller). Within the fibers of the rhomboid ligament.[13] Not constant. May simulate a costoclavicular articulation, of which, indeed, it seems to be the beginning.

B. submammaria. Between the mammary gland and the pectoralis major. Rare, but interesting, as it may be involved in a case of mammary abscess.

B. anguli sterni. Subcutaneous over the angle between the first and second pieces of the sternum. In carpenters and cabinetmakers.

B. hyperziphoidea. Subcutaneous over xiphoid cartilage. Usual in shoemakers and rachitic children.

B. suprapubica. Beneath the pubic attachment of the rectus abdominis. Duval[14] reports that inflammation of this has been known to occur as a sequel to croupous pneumonia. Not mentioned by authorities generally. Schreger mentions a subcutaneous bursa at the side of the suspensory ligament of the penis.

B. costæ primæ. Between the muscles of the back and the tuberosity of the first rib. Mentioned by Nancrede. It is probably rare, as the principal authorities omit it.

B. subcutanea sacralis (Luschka). Over spinous process of fourth or fifth sacral vertebra, or over the articulation of the sacrum and coccyx. Usual in old subjects.

B. coccygea (Luschka). Between tip of coccyx and sphincter ani. Common.[15]

B. phrenicohepatica anterior (von Brunn[16]). Between the left lateral ligament of the liver and the under surface of the diaphragm in front. Found in 31 cases out of 64. Its enlargement might simulate a diaphragmatic hernia.

B. phrenicohepatica posterior (von Brunn). Between the same structures behind. Found in 2 cases out of 64.

SHOULDER.—*B. musculi trapezii.* Between the aponeurotic part of the trapezius and the base of scapular spine (3 times in 12, Synnestvedt).

B. spinæ scapulæ, B. supracromialis. These are subcutaneous, found in those who carry burdens.

B. infrascapularis. Between the inferior angle of the scapula and the chest wall. Usually between subscapularis and serratus magnus. May be of considerable size, and by crepitation, when inflamed, simulate crepitant râles or pleuritic fremitus.[17]

B. subdeltoidea (Fig. 1173). Between the under surface of the acromion + structures arising therefrom (lateral portion of coracoacromial ligament, deltoid muscle) and the capsular ligament of the shoulder joint.[18] Constant. Many authors describe the upper part of this bursa separately as *B. subacromialis.* This portion may be separate, but it usually communicates, and the whole should be considered as a single large multilocular bursa. Rarely communicates with the joint. Its inflammation may simulate dislocation of the biceps tendon (Nancrede).

B. musculi coracobrachialis (Monro). Between the lateral part of the subscapularis and the short head of the biceps + coracobrachialis. Sometimes communicates freely with B. subdeltoidea. Also known as B. subcoracoidea.

B. m. coracobrachialis minoris (Gruber). Under a rare muscle, which arises from the anterior and internal part of the coracoid process.

B. fossæ infraclaviculares (Gruber) (Fig. 1173). Between two layers of the coracoclavicular fascia costocoracoid membrane), in front of the coracoid process. Frequent (1 in 3), more common in women.

B. coracoclavicularis media (Gruber) (Fig. 1173). Between the conoid and the trapezoid ligaments. Frequent (1 in 2). May simulate a coracoclavicular articulation.

B. coracoclavicularis lateralis (Gruber) (Fig. 1173). Between the coracoid process and the trapezoid ligament. Occasional (1 in 5).

B. subtendinea m. pectoralis minoris. Under insertion of pectoralis minor. Rare (1 in 30 or 40, Gruber).

B. vaginalis pectoralis minoris (Gruber) (Fig. 1173). Around tendon of pectoralis minor. Rare (1 in 10).

B. musculi subscapularis (Fig. 1173). Between the subscapularis and the neck of the scapula. Constant. It always communicates with the joint, and may properly be considered as a diverticulum of the capsule.

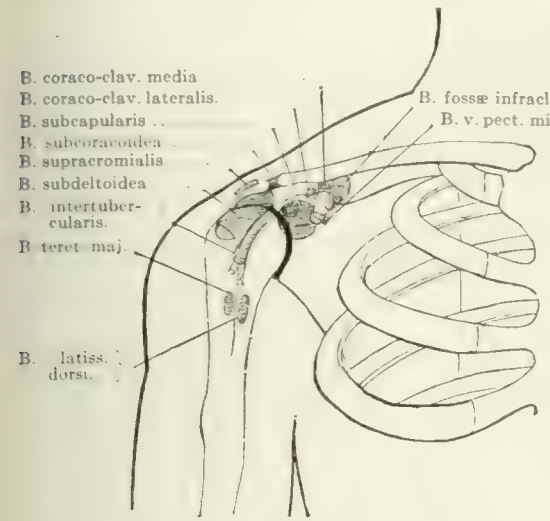

Fig. 1173.—The Principal Bursæ about the Shoulder.

B. subcoracoidea (Gruber) (Fig. 1173). Between the upper edge of the subscapularis and the B. subscapularis.[19] Found 10 out of 12 times (Synnestvedt); in two of these cases it communicated with B. subscapularis.

B. subtendinea subscapularis (Synnestvedt). Between the tendon of the subscapularis and the capsule (2 times in 18).

B. intertubercularis (Henle[20]) (Fig. 1173). Surrounding the tendon of the long head of the biceps in the groove of the humerus. Constant. Always communicates with joint cavity, and should be considered as a diverticulum of the capsule.

B. musculi infraspinati (Rosenmüller). Between upper edge of infraspinatus and scapular spine (2 in 3, Synnestvedt).

B. subtendinea m. infraspinati. Between tendon of infraspinatus and capsule (4 in 14, Synnestvedt).

B. subtendinea m. teretis minoris (Gruber). Under the tendon of the teres minor. Rare.

B. musculi teretis majoris (Fig. 1173). Between the tendon of insertion of the teres major and the latissimus dorsi. Constant.

B. musculi latissimi dorsi (Fig. 1173). Between the tendon of the latissimus dorsi and the humerus.

B. musculi pectoralis majoris. Between tendon of pectoralis major and B. intertubercularis + tendon of latissimus dorsi (4 in 12, Synnestvedt).

B. intermuscularis pectoralis majoris (Synnestvedt). Between the clavicular and thoracic portions of the muscle.

Elbow.—*B. bicipitoradialis* (Rosenmüller). Between the tendon of the biceps and the tuberosity of the radius. Constant, often double.

B. cubitalis interossea (Jancke). Between the tendon of the biceps + radial tuberosity and outer surface of ulna + muscles of that region. Of considerable size. Frequent (1 in 4, Gruber; 3 in 6, Synnestvedt).

B. subtendinea m. brachialis. Between the tendon of insertion of the brachialis muscle and the coronoid process. Rare. The older anatomists (Fourcroy, Jancke, Koch) describe a bursa between the brachialis and the interosseous ligament.

B. m. flexoris digitorum sublimis (Gruber). Under the tendon of origin of the flexor sublimis, or between it and the pronator radii teres. Very rare (1 in 200).

B. m. palmaris longi. Between the origin of the muscle and the joint capsule. Very rare.

B. subcutanea olecrani (Camper). Between the skin and the olecranon covered by the tendon of the triceps. Constant in adults.

B. subtendinea olecrani. Between the tendon of the triceps and the olecranon and the posterior ligament of the elbow joint. Frequent (3 in 5); constant in old subjects.

B. intratendinea olecrani. Within the tendon of the triceps. Quite frequent (7 in 12, Synnestvedt).

B. humerotricipitalis. Between the anterior surface of the triceps and the fat covering the lower end of the humerus. Rare (1 in 12, Synnestvedt).

B. retroepitrochlearis. Between the triceps + ulnar curve behind, and the posterior surface of the internal condyle + median surface of capsule in front. Very rare.

B. m. anconei (Rosenmüller). Between the anconeus and the capsule (1 in 4 or 5). May communicate with B. extensoris carpi ulnaris or with joint (Henle).

B. subcutanea epicondyli lateralis (Schreger). Between the skin and the external condyle of the humerus. Rare (1 in 60).

B. m. extensoris carpi ulnaris (Jancke). Under origin. May extend under the extensor communis. Frequent (1 in 3 or 4). May communicate with the joint and also with B. anconei.

B. m. extensoris carpi radialis brevis (Monro). Between the common origin of the extensor carpi radialis brevis + the extensor communis digitorum and the head of the radius (1 in 6 or 7).

B. subcutanea epicondyli medialis (Schreger). Between the skin and the inner condyle of the humerus. Rather frequent (1 in 5).

Wrist and Hand.—*B. ulnaris subcutanea.* Over styloid process of ulna. Not constant (3 in 11, Synnestvedt).

B. radialis subcutanea. Over styloid process of radius. Rather rare.

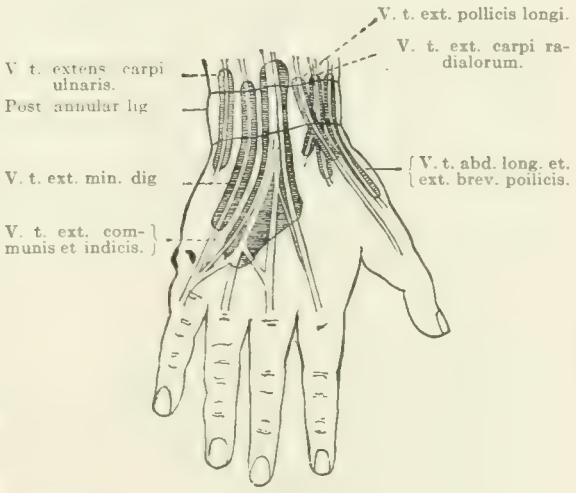
V. t. ext. pollicis longi.
V. t. ext. carpi radialorum.
V. t. extens. carpi ulnaris.
Post. annular lig.
V. t. ext. min. dig.
V. t. ext. communis et indicis.
V. t. abd. long. et ext. brev. pollicis.

Fig. 1174

B. dorsalis carpiea subcutanea. Schreger found this in 2 cases.

Vagina tendinis m. extensoris carpi ulnaris (Fig. 1174). A small sheath. Reaches to the base of metacarpale V.

Vagina tendinis m. extensoris digiti minimi (Fig. 1774). A small and separate sheath.

Vagina tendinum mm. extensoris digitorum communis et extensoris indicis (Fig. 1174). Large. Extends farther toward the fingers on the ulnar side.

Vagina tendinis musculi extensoris pollicis longi (Fig. 1174). Runs obliquely across the next.

Vagina tendinum mm. extensorum carpi radialium (Fig. 1174). In groove on back of radius. Single above, divides below.

B. subtendinea m. extensoris carpi radialis longi. Under the tendon at its insertion into metacarpale II. (4 in 20, Synnestvedt).

B. subtendinea m. extensoris carpi radialis brevi. Under the tendon at its insertion into metacarpale III. (18 in 20, Synnestvedt).

Vagina tendinum abductoris longi et extensoris brevis pollicis (Fig. 1174).—Surrounds these tendons from the dorsal surface of the radius to the outer edge of the wrist.

B. musculi flexoris carpi ulnaris (Fig. 1175). Under the tendon at its insertion into pisiform (6 in 30, Synnestvedt).

Vagina tendinum mm. flexorum communium (Fig. 1175). The usual arrangement of this extensive sheath is to surround the tendons of both the superficial and deep flexors as they lie in the wrist and palm, sending a diverticulum downward upon the tendons of the little finger. Schüller[21] describes this bursa as double, the sheath for the tendons of digits IV. and V. being separate from those of digits II. and III. Holden[22] reports a case in which this bursa communicated with the wrist joint. It does not usually communicate with the radial bursa,[23] but many varieties are found.[24]

B. musculi flexoris carpi radialis (Fig. 1175). In the groove of the trapezium.

Vagina tendinis m. flexoris pollicis longi (Fig. 1175). Extends from an inch above the anterior annular ligament to the base of the second phalanx of the thumb, upon the tendon of the flexor longus pollicis.

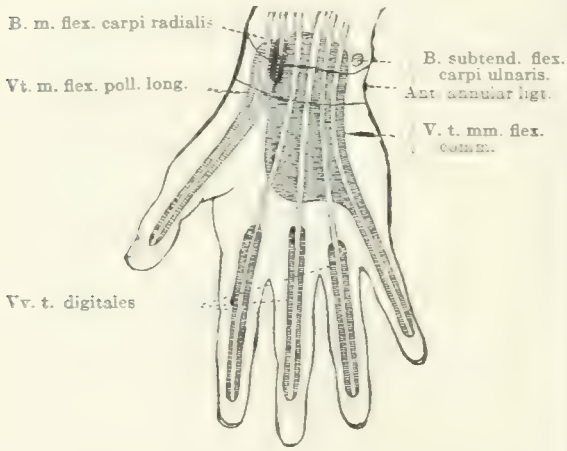

FIG. 1175.

Bb. metacarpophalangeæ dorsales subcutaneæ. Between the skin and the extensor tendons on the ulnar side over the metacarpophalangeal joint (Synnestvedt found them in digit I., 40 per cent.; digit II., 53 per cent.; digits III. and IV., 66 per cent.; digit V., 27 per cent.).

Bb. subcutaneæ digitorum dorsales. Between the skin and the proximal joints of the fingers. Quite constant.

Bb. dorsales subtendineæ.—Between the tendons the capsules of the metacarpophalangeal joints. Quite constant. Frequently communicate with joint. When not found a diverticulum of capsule takes the place (Theile, Synnestvedt).

Bb. volares articuli metacarpophalangei. Between the skin + subcutaneous fat and the flexor tendon with its fibrous sheath. Found by Schreger in all the digits, by Synnestvedt only in digits I., II., and III.; most frequent in digit III.

Bb. volares phalangis primæ. Between the skin and subcutaneous tissue and the flexor tendon with its sheath in front of the first phalanx. Found by Synnestvedt in but two instances, in digit II. and digit III.

Vaginæ tendinum digitales (Fig. 1175). Special sheaths for the flexor tendons of digits II., III., and IV.

Bb. intermetacarpophalangea. Between the heads of metacarpales II., III., IV., and V.

Bb. interossea. Between the tendons of the interossei muscles and the metacarpophalangeal joints. Gruber[25] finds two sets of these, one under the part of the tendon that extends to the dorsal aponeurosis, the other under the part which communicates with the phalanx.

B. metacarpea ulnaris (Synnestvedt). Between the skin and the head of the fifth metacarpal. Found in 8 out of 15 cases.

HIP.—*B. iliaca anterior.* Subcutaneous over the anterior superior spine of the ilium.

B. iliopectinea. Under the tendon of the iliopsoas, covering the iliopectineal tubercle, the anterior surface of the pubis, and the capsule of the hip joint. This large and constant bursa is sometimes multilocular and frequently (6 in 14, Synnestvedt) communicates with the hip joint.

B. iliaca subtendinea. Between the tendon of insertion of the iliopsoas and the femur. Not constant.

B. pectinei. Between the insertion of the pectineus and the femur + lowest fascicles of the iliacus. Frequent (8 in 14, Synnestvedt).

B. trochanterica subcutanea. Between the skin and the lateral surface of the great trochanter. Usually small, but sometimes multilocular. Rather frequent (4 in 13, Synnestvedt).

B. trochanterica m. glutei maximi. Between the tendon of the gluteus maximus and the posterior and external portions of the great trochanter. Large and constant; frequently multilocular.

Bb. gluteofemorales. One or more between the tendon of the gluteus maximus and the femur. Quite constant.

B. gluteofascialis. Between the tendon of the gluteus maximus and the origin of the vastus internus. Constant.

B. trochanterica musculi glutei medii anterior. Between the anterior portion of the tendon of the gluteus medius and the great trochanter. Nearly constant (12 in 15, Synnestvedt).

B. trochanterica m. glutei medii posterior. Between the posterior portion of the tendon of the gluteus medius and the pyriformis. Usual (10 in 15, Synnestvedt).

B. trochanterica m. glutei minimi. Between the gluteus minimus and the anterior surface of the great trochanter. Large and nearly constant (14 in 15, Synnestvedt).

B. m. recti femoris. Between the reflected tendon of the rectus and the upper edge of the acetabulum (5 in 16, Synnestvedt).

B. m. pyriformis. Under the distal insertion of the muscle. Infrequent (3 in 12, Synnestvedt).

B. gemellorum (Synnestvedt). Between the gemelli and the joint capsule. Found once only. It communicated with B. circumflexa.

B. m. obturatoris interni. Between the tendon of the obturator and the gemelli. Rather frequent (5 in 13, Synnestvedt). Communicates sometimes with B. circumflexa.

B. circumflexa m. obturatoris interni. Between the muscle and the lesser sciatic notch.

B. subtendinea m. obturatoris interni. Between the tendon and the capsule of the hip joint. Rare. May communicate with last (Quain).

B. m. obturatoris externi (Synnestvedt). Between the obturator externus and the joint capsule. Infrequent (2 in 18).

B. m. quadrati femoris. Between the quadratus femoris and the trochanter minor + tendon of iliopsoas. Constant.

B. subcutanea tuberis ischii. This is described by some (Hyrtl, Nélaton) as directly under the skin over the tuberosity of the ischium. It is probably rare. The three following are often mistaken for it:

B. ischiadica musculi glutei maximi. Between the lower border of the gluteus maximus and the tuberosity of the ischium (5 in 12, Synnestvedt.)

B. m. bicipitis femoris superior. Between the tendon of the united semitendinosus and biceps and the tuberosity. Constant.

Bb. m. semimembranosæ in tubere ischii. Two of these are found between the tendon of the semimembranosus and the quadratus femoris. One is quite constant (9 in 12), the other infrequent (2 in 12, Synnestvedt).

B. iliaca posterior. Subcutaneous over the posterior superior spine of the ilium.

KNEE.—*B. condyli medialis;*

B. condyli lateralis. Subcutaneous bursæ over the projecting condyles (Figs. 1176 and 1177).

B. præpatellaris subcutanea (Fig. 1176). In the subcutaneous connective tissue in front of the patella. This is quite common (18 in 20, Synnestvedt; 165 in 400, Gruber), and is usually confounded with the next. It may be of considerable size.

B. præpatellaris subfascialis. Between the fascia in front of the patella and the aponeurosis of the extensors. Not so frequent (9 in 20, Synnestvedt; 23 in 400, Gruber).

B. præpatellaris subtendinea. Between the aponeurosis and the anterior surface of the patella. Found in 9 out of 20, Synnestvedt; 23 in 400, Gruber; 10 out of 12, Schreger. This division of the prepatellar bursæ is that of Gruber. The three here described

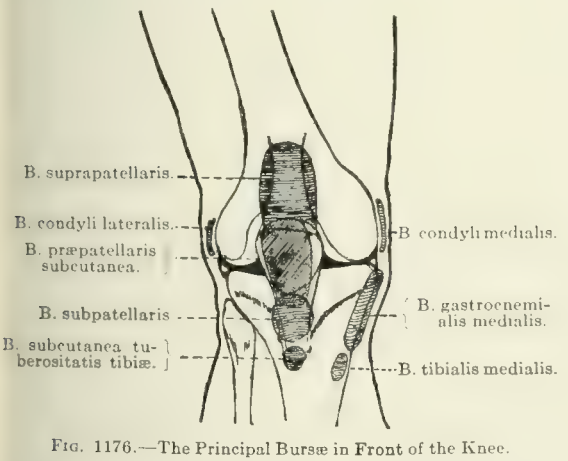

FIG. 1176.—The Principal Bursæ in Front of the Knee.

rarely coexist, and if so they usually communicate.

B. suprapatellaris (Fig. 1176). Between the tendon of the extensor quadriceps and the lower part of the anterior surface of the femur above the patella. This is always present, and invariably communicates with the joint, except occasionally in very young children.

B. intermuscularis m. extensoris cruris. Between the tendons of rectus and the crureus. About an inch above the patella. Rare (2 in 55, Synnestvedt).

B. patellaris lateralis. Between lateral expansions of the tendons of the quadriceps femoris and the patella. Rare.

B. patellaris lateralis interna. In a similar situation on the inner side. Synnestvedt mentions two varieties, one superficial and one deeper.

B. infrapatellaris subcutanea. Between the fascia and the ligamentum patellæ. (Found by Synnestvedt in 6 out of 15.)

B. subcutanea tuberositatis tibiæ (Fig. 1176). Between the skin and the tuberosity of the tibia. Usual in old subjects.

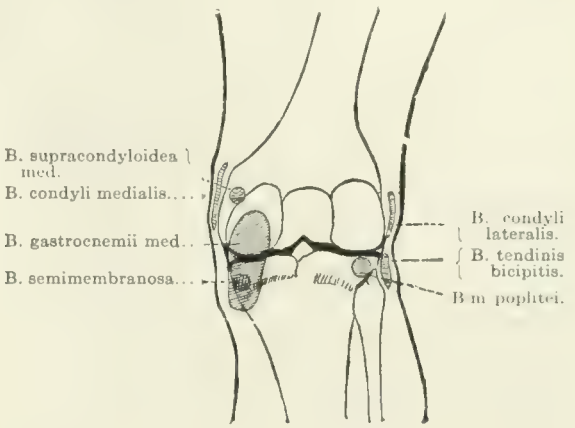

FIG. 1177.—The Principal Bursæ Behind the Knee.

B. infrapatellaris profunda (Fig. 1176). Between the ligamentum patellæ and the anterior surface of the tibia. Constant and large. May occasionally communicate with the joint, though Synnestvedt has never seen this, and thinks the reported cases erroneous.

B. musculi sartorii propria. Between the tendon of the sartorius and the gracilis and semitendinosus muscles. Rather rare (2 in 15, Synnestvedt).

B. sub ligamento mediale (Synnestvedt). Between the internal lateral ligament and the capsule (11 out of 21).

B. anserina. Between the expansion of the lower internal ham-string tendons (semitendinosus, gracilis, sartorius), and the long internal lateral ligament.[26] Constant. It occasionally blends with B. gastrocnemialis interna, and through that communicates with the joint.

B. tibialis subcutanea (Schreger). Subcutaneous over upper end of tibia. Not found by Gruber or Synnestvedt.

B. tendinis m. poplitei. Between the external lateral ligament and the tendon of the popliteus. Not constant (5 in 16, Synnestvedt). Occasionally communicates with joint.

B. m. bicipitis inferior (Fig. 1177). Between the external lateral ligament and the tendon of the biceps. Nearly constant (21 in 26, Synnestvedt; 191 in 200, Gruber). It occasionally communicates with the joint. The external popliteal nerve is in relation with it.

B. subtendinea m. tensoris fasciæ latæ (Synnestvedt). Between the iliotibial band and the capsule. Found in 3 out of 19, once communicating with joint.

B. fibularis subcutanea (Schreger). Subcutaneous over upper end of fibula. Not found by Gruber or Synnestvedt.

B. supracondyloidea medialis (Fig. 1177). Between the inner tendon of the gastrocnemius and the femur. Nearly constant. May communicate with joint.

B. musculi gastrocnemii medialis (Figs. 1176 and 1177). Between the inner head of the gastrocnemius and the semimembranosus. It is behind the internal condyle and over the neighboring capsule. Large and

constant. Sometimes multilocular. In adults it usually communicates with the joint. Synnestvedt describes the lower part of this as a separate bursa, under the name of *B. semimembranosogastrocnemialis.*

B. m. semimembranosi (Fig. 1177). Between the expansion of the semimembranosus tendon and the inner condyle of the tibia. Usually closed. Constant.

B. m. gastrocnemii lateralis. Between the external head of the gastrocnemius and the capsule. Rare.

B. bicipitogastrocnemialis. In the popliteal groove between the prominence of the sesamoid bone in the head of the gastrocnemius and the biceps tendon. Very rare.

B. m. poplitei (Fig. 1177). Between the popliteus and the joint capsule + external tuberosity of tibia. This always communicates with the joint, and is properly a diverticulum of the capsule, occasionally (1 in 10, Lenoir) it also communicates with the cavity of the superior tibiofibular articulation.

Ankle and Foot.—*B. subcutanea malleoli lateralis; B. subcutanea malleoli medialis.* Subcutaneous over the malleoli. Not constant. External more frequent.

Vaginæ tendinum m. extensoris digitorum pedis longi; Vag. tendinis m. extensoris hallucis longi;

Vag. tendinis m. tibialis anterioris (Fig. 1178). Around the tendons of these muscles. Not infrequently the sheath of the extensors extends somewhat higher up than is shown in the figure.

B. sinus tarsi (Gruber). Between the fascia which binds down the extensor longus digitorum and the head of the astragalus. Quite frequent (5 in 12, Synnestvedt; 97 in 174, Gruber). May communicate with joint.

Bb. sub musculo pediæo. Under the extensor brevis digitorum. Usually two. Found by Synnestvedt 2 in 16.

B. tarsiea subcutanea (Schreger). On dorsal surface of foot.

Vagina tendinis m. tibialis posterioris (Fig. 1179). Surrounds the tendon as it lies back of the internal malleolus.

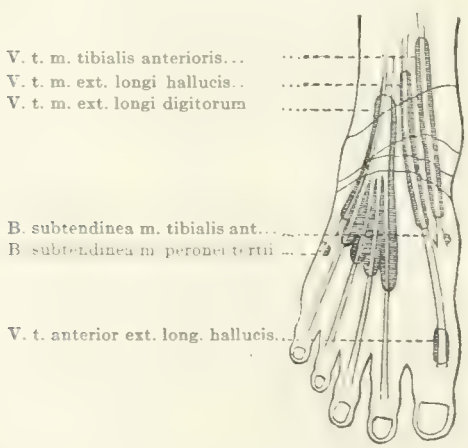
V. t. m. tibialis anterioris
V. t. m. ext. longi hallucis
V. t. m. ext. longi digitorum
B. subtendinea m. tibialis ant.
B. subtendinea m. peronei tertii
V. t. anterior ext. long. hallucis

Fig. 1178.—Synovial Sheaths on Back of Ankle and Foot.

Vaginæ tendinum m. flexoris digitorum longi and *Vag. tendinis m. flexoris hallucis longi* (Fig. 1179). Surround the tendons behind the internal malleolus and extend into the sole.

B. subcutanea calcanea. Between the tendon and the deep fascia. Not constant.

B. tendinis calcanei (Fig. 1179). Between the tendon and the posterior surface of the calcaneum. Constant. Has cartilage on two of its walls, viz., over the bone, and a thin layer coating the anterior surface of the tendon.

B. subcalcanea (Lenoir[27]). Between the inferior surface of the calcaneum and the plantar fascia. Constant.

B. subtendinea musculi tibialis anterioris (Fig. 1178). Under the tendon at its insertion upon cuneiforme I. (5 in 12, Synnestvedt).

B. subtendinea m. tibialis posterioris. Between the tendon and the navicular bone.

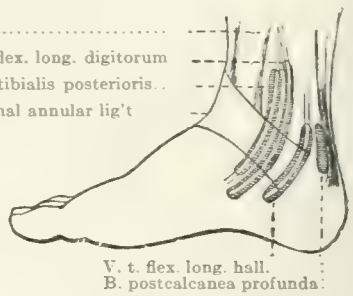

Fig. 1179.—Synovial Sheaths of Inner Side of Foot.

Bb. m. abductoris minimi digiti (Synnestvedt). One between the abductor and the sesamoid bone of the peroneus longus; another between the muscle and the tuberosity of metacarpale V. Rare.

B. subtendinea m. peronei tertii (Hyrtl) (Fig. 1178). Under the tendon at its insertion upon head of metacarpale V. Not constant.

B. subtendinea m. extensoris longi hallucis. Between the tendon and the head of metacarpale I. Small and rather rare.

Vag. tendinis anterior extensoris hallucis longi (Fig. 1178). Over metatarsophalangeal joint I. About one inch long.

Vag. tendinum mm. peroneorum communis. Sheathes the peroneal tendons behind the external malleolus. Single in the middle, it divides above and below.

Bb. dorsales subcutaneæ. Several of these are described by Schreger and Synnestvedt. One over cuneiforme I., one over head of metacarpale I., and occasionally over other projections.

Bb. dorsales subtendineæ (Synnestvedt). These occur in similar situations as those of the hand, and agree with them in form and size.

Vag. tendinis m. peronei longi plantaris. Sheathes the tendon as it lies in the groove of the cuboid. A small bursa is sometimes found under the tendon where it turns around the outer side of the cuboid, and another under its insertion upon metatarsale I.

Bb. plantaris metatarsophalangei (Schreger). These occur at the articulations.

B. plantaris in capitulo ossis metatarsi I. (Lenoir); *B. plantaris in capitulo ossis metatarsi V.* (Lenoir). These are well-known bursæ between the skin and the points of greatest pressure.

Bb. intermetatarsophalangeæ. These are usually found in old subjects, between the toes, in the region of the metatarsophalangeal joints. The three inner are most constant (No. 1, 95 per cent.; No. 2, 98 per cent.; No. 3, 95 per cent.; No. 4, 28 per cent., Gruber). Occasionally communicate with joints.

Bb. m. interosseorum. Between the interossei and the metatarsophalangeal joint. Rarely communicate.

Bb. mm. lumbricalium pedis. Under the lumbricales and laterally to them. Rare.

B. abductoris minimi digiti. Between the abductor of the little toe and the head of metatarsale V. Rare (1 in 14, Synnestvedt).

Bb. phalangea dorsales (Schreger). These are not so constant as those of the hand.

Vaginæ tendinum digitalium pedis. Surround the tendons of the flexor muscles in the sole of the foot.

Frank Baker.

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Burseraceæ.—A small, but rather important family of some sixteen genera and about two hundred species, distributed through all tropical and some subtropical regions. A few fruits are somewhat eaten (Protium), and some of the seeds yield useful fixed oils. The principal value of the family resides in its numerous gum resins and oleoresins, which have from the earliest times been used for incense and recognized as important articles of commerce. The best known of them are myrrh, bdellium, olibanum, and elemi, discussed elsewhere, which represent the constituents and properties of the family. Henry H. Rusby.

Bursitis.—It is generally thought that all bursæ are the same in structure, but this is probably not so. "The bursæ may be either deep-seated or subcutaneous. The former are for the most part placed between a muscle or its tendon, and a bone or the exterior of a joint, less commonly between two muscles or tendons. The subcutaneous lie immediately under the skin, and are found in various regions of the body interposed between the skin and some firm prominence beneath it. It must, however, be observed that, amongst these subcutaneous bursæ, some are reckoned which do not always present the characters of true synovial sacs, but look more like

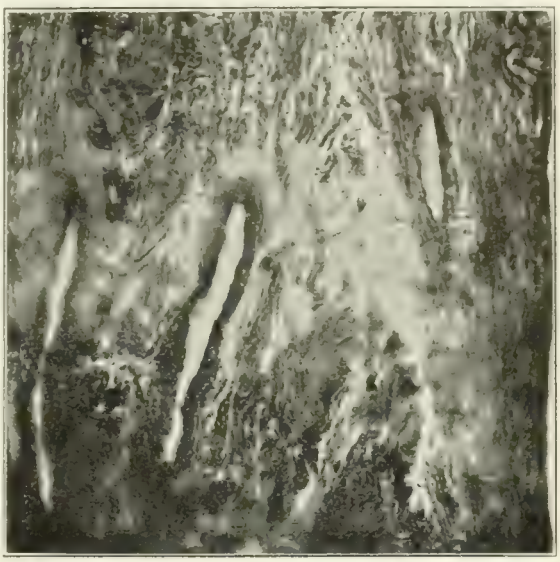

Fig. 1180.—Section of Normal Joint Capsule; rather highly magnified. The "lymph spaces" show well in this photomicrograph, but the peculiar cells on the surface of the membrane show very poorly.

mere recesses in the subcutaneous areolar tissue, larger and more defined than the neighboring areolæ, but still bounded by an evident synovial membrane." (Quain's Anatomy.)

My investigations, by no means extensive, incline me to the belief that the bursæ found in the region of the joints, and where tendons or muscles play over a bony prominence or upon each other, are true synovial cavities, *bursæ synoviales*, while those found subcutaneously over bony prominences, *bursæ mucosæ*, have a different structure. In the latter category fall such bursæ as the prepatellar, and probably also those that are developed in the subcutaneous tissue as the result of constant trauma — "adventitious bursæ."

Synovial Bursæ.—These often communicate with the cavity of a joint, and may be involved in joint disease. They are vulnerable to the same diseases as are the synovial membranes of joints, and the etiology, pathology and treatment of bursitis are therefore much the same as are those of arthritis. They are often acutely affected by trauma also. Thus, an acute suppurative inflammation demands incision and drainage; tuberculosis, excision; acute traumatic bursitis, rest, hot and cold applications, and strapping. Occasionally one sees a subacute form which apparently is caused by an obscure infection somewhere else in the body, and which resists treatment until the source of infection is removed. The diagnosis is made on much the same points as would be the diagnosis of disease of the joint synovia, plus the location of the trouble at the known situation of the bursa. Localized pain, swelling, and fluctuation are

present, and if the inflammation be due to pus cocci, redness and heat are added.

Mucous Bursæ.—These bursæ are wont to enlarge and fill with fluid as the result of oft-repeated trauma, and often are formed *de novo* in unusual situations as the result of such trauma. According to Langemak[1] the enlargement is to be regarded as simply an exaggeration of the process which originated the bursa. According to this author the pathological process is not an inflammation, but a collagenous degeneration

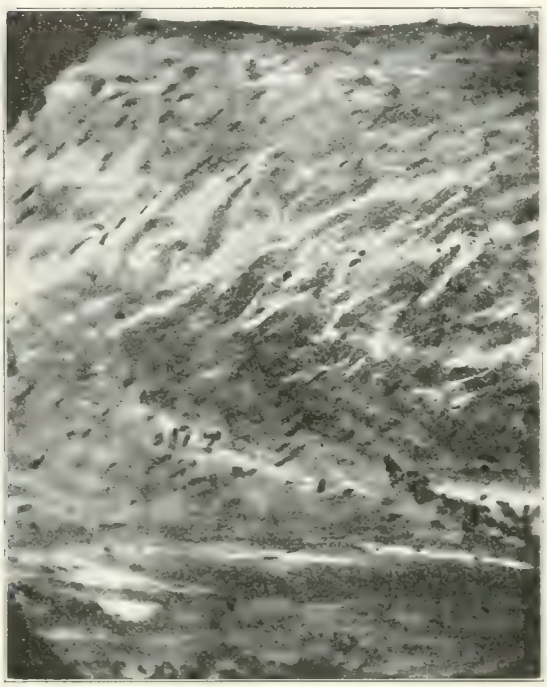

Fig. 1181.—Section of Wall of Normal Prepatellar Bursa; same magnification as Fig. 1180. Compare the two photomicrographs. The structures are entirely different.

—an hygroma. The hygroma may later become secondarily infected. Some writers maintain that it is prone to syphilitic degeneration. A simple hygroma is filled with fluid or with gelatinous material, is painless, slow of growth, and usually fluctuates. When secondarily infected it is painful, and presents signs of active inflammation. The treatment consists in extirpation of the sac. Sometimes, if the cause of enlargement can be removed, aspiration and pressure may be efficacious.

"House-maid's knee" is the term applied to prepatellar bursitis, "miner's elbow" to olecranon bursitis, "weaver's bottom" to gluteal bursitis. Tailors develop an enlarged bursa over the external malleolus. An adventitious bursa developing over the metatarsophalangeal joint of the great toe constitutes the familiar bunion.

Individual Forms of Bursitis.—*Prepatellar bursitis* is found most often among those whose occupation requires kneeling. It is slow and chronic, fluctuates, is usually painless if uninfected, and is situated over the patella, more especially over its lower half. The treatment consists in eradication of the sac, with care not to open the knee-joint at the sides of the patella. If a syphilitic element be present, the appropriate remedies must be used in addition.

Subpatellar Bursitis.—Inflammation of the bursa under the patellar tendon, subpatellar bursitis, shows itself as a fluctuating swelling on either side of the tendon. Incision and drainage may be necessary. The disease must be differentiated from injury of the tibial tubercle sometimes seen in adolescents.

The bursa between the tendons of the semimembranosus and the inner head of the gastrocnemius communicates with the knee-joint in about fifty per cent. of cases. This fact must be borne in mind in operations upon it.

Bunion.—Probably as the result of ill-fitting shoes, the proximal phalanx of the great toe is thrust outward and is subluxated on its metatarsal bone—*hallux valgus*. Over the enlarged metatarsophalangeal joint a bursa forms, which by pressure becomes painful, and frequently becomes infected. Palliative treatment of the milder forms consists in relief of pressure, and in proper shoes. The frequently accompanying (and causal) flat-foot requires attention. For the severer grades excision of the head of the metatarsal, or of part of it, will usually be necessary. If secondarily infected, the bursa must first be opened and drained. Thereafter shoes built on proper lines must be worn, and perhaps a flat-foot brace in addition. Some operators transplant the extensor tendon of the great toe.

A bursa often develops under a corn, and its secondary infection may give rise to great pain and even to constitutional disturbance. It is these bursæ which often make a corn extremely sensitive. Relief of pressure by proper shoes, or, when the corn is on the

Fig. 1182.—Prepatellar Bursitis ("Housemaid's Knee").

sole of the foot, by a sole plate, will usually cure the uninfected cases. Secondary infection demands incision and drainage.

Retrocalcaneal Bursitis.—Injury of this bursa is often followed by extreme sensitiveness over the back of the heel between the tendo Achillis and the calcaneus. Fluctuation may be distinguished at the sides of the tendon. Treatment is usually by a

long strip of adhesive strapping from the upper part of the back of the calf, under the heel to the ball of the foot, put on while the foot is plantar-flexed, and reinforced by criss-cross strapping over the heel. Chronic inflammation of this bursa often accompanies flat-foot and yields to the treatment of the causal affection. Areas of calcification are said to exist in the chronic forms of inflammation of this bursa.

Tailors occasionally develop an adventitious bursa over their external malleoli. It should be excised if it becomes troublesome.

Iliopsoas Bursitis.[2]—The iliopsoas bursa communicates with the hip-joint in a fair proportion of cases (3 out of 18, according to Lund) and inflammation of it may evidence itself as a fluctuating tumor in front of the joint capsule to the outside of the femoral vessels.

Olecranon Bursitis.—"Miner's elbow" may be said to be an analogous disease to prepatellar bursitis. The treatment is the same—usually excision.

Subacromial or Subdeltoid Bursitis.—This was described some years ago by Duplay, but its full importance was not realized until the researches of Codman, of Boston, placed its pathology and symptomatology on a sound footing. It is now recognized as the cause of many of the cases of stiff and painful shoulders that formerly defied treatment. This bursa, when the arm is at the side, lies about half under the deltoid muscle and half under the acromion. When the arm is fully abducted the bursa is almost entirely subacromial. Codman maintains that its size is usually about that of a silver dollar.

Etiology.—The bursa may be involved in any of the infectious processes we have enumerated, and also attracts peculiar attention by its liability to injury. The injury is usually a fall upon the shoulder, or a sudden active abduction of the arm. The bursa may contain fluid or its walls may be more or less glued together. Sometimes the tendon of the supraspinatus is torn near its attachment. A condition similar to subacromial bursitis often results after dislocation of the head of the humerus, when the greater tuberosity has been torn off and has been allowed to heal in a faulty position. In the past many of these cases were diagnosed vaguely as "periarthritis," circumflex neuritis, injury to the brachial plexus, heumatism, etc., but Codman has shown their true nature.[3]

Symptomatology.—Localized pain and sensitiveness over the bursa are almost always present, and the pain may shoot down the arm. The main diagnostic point is a *limitation of motion in the direction of abduction and of external rotation.* Atrophy of the deltoid may be present. Of course, the bursa may be involved in shoulder-joint disease, but in bursitis pure and simple a skiagram will not show any disease of the joint itself or of the head of the bone. Possibly small areas of calcification may appear in the bursa.

The main difficulty in diagnosis will lie in the differentiation of this lesion from disease of the shoulder-joint and from fracture, and a skiagram will be our most useful aid.

The treatment of the traumatic form will vary somewhat as the severity of the disease. Mild cases may recover in a short time under hot and cold applications, gentle massage, and possibly a position of the shoulder-joint at right-angle abduction. Sometimes in the resistant cases, breaking up of the adhesions under ether may be necessary, followed by persistent massage and passive motion. In the very severe cases, removal of the subdeltoid portion of the bursa has been highly recommended.[4]

T. Turner Thomas[5] has disputed the important rôle of the subacromial bursa in injuries about the shoulder-joint, and ascribes the symptoms to a tearing of the capsular ligament on the axillary side of the joint, by forced abduction of the arm. He maintains his argument with some force. LEONARD W. ELY.

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4. Baer: Johns Hopkins Bulletin, 1907, pp. 195–196. Painter, Boston Medical and Surgical Journal, March 21, 1907.
5. T. Turner Thomas: Therapeutic Gazette, February, 1912. American Journal of the Medical Sciences, April, 1911.

Buthus.—A genus of scorpions, family *Scorpionidæ. B. carolinus* is the common species in the southern United States. It has a poisonous sting at the end of the slender abdomen but the wounds it inflicts are usually not serious. See *Arachnida.*

A. S. P.

Butneria.—See *Calycanthus.*

Butternut.—See *Juglans.*

Button Scurvy.—See *Ecphyma Globulus.*

Butyl Chloral Hydrate.—$C_4H_5Cl_3O,H_2O$. This substance, formerly erroneously styled *croton chloral hydrate,* was introduced into medicine in 1870 by Liebreich, but has not met with much favor, and has failed to secure official recognition in the United States Pharmacopœia; it is, however, official in the British Pharmacopœia. Butyl chloral hydrate is in the form of colorless crystalline scales, of an odor and taste reminding of ordinary chloral hydrate. It has the disadvantage, as compared with the latter substance, of being but sparingly soluble in cold water. It dissolves freely in alcohol, in glycerin, and in boiling water.

Butyl chloral hydrate is closely allied, chemically, to ordinary chloral hydrate and resembles that compound in its effects upon the animal system. Its only recommendation to medical favor lay in its supposed property of being peculiarly anodyne to the trigeminal nerve (Liebreich), and so of peculiar promise for the alleviation of neuralgias of the face and head, including neuralgia due to decayed teeth; but this property certainly does not exist to any marked degree. Practically, the drug is only a comparatively insoluble, and therefore inconvenient, substitute for ordinary chloral hydrate. It may be given in doses ranging from gr. v. to xxx. (0.30 to 2.0) in syrupy mixture. EDWARD CURTIS.
R. J. E. SCOTT.

Butyric Acid, $C_3H_7.COOH$, occurs in the animal organism under a variety of conditions. It is chiefly characteristic of butter, being found there in the form of an ester, a triglyceride, and as such constitutes the chief fat of butter and milk. To butyric acid set free by fermentation is due the peculiar rancid taste and odor of contaminated butter. When milk sours, milk sugar (lactose) is converted into lactic acid by the lactic ferment of various bacteria in accordance with the following equation.

$$\underset{\text{Lactose}}{C_{12}H_{22}O_{11}} + H_2O = 4\underset{\text{Lactic acid}}{C_3H_6O_3}$$

The lactic acid is then acted upon by butyric acid ferment contained in the air.

$$\underset{\text{Lactic acid}}{2C_3H_6O_3} = \underset{\text{Butyric acid}}{C_4H_8O_2} + 2CO_2 + 2H_2$$

Butyric acid in pure condition is a strongly acid liquid, mixing with water in all proportions and having a boiling point of 163° C. It may be present in the gastric contents under abnormal conditions, viz., with a markedly diminished hydrochloric acid secretion. In excessive fermentation in the enteric tract butyric acid may be formed in significant amounts. FRANK P. UNDERHILL.

Buxton.—Buxton, situated in the Peak district of Derbyshire, England, at an elevation of about 1,000 feet above sea-level, is a pleasant and popular resort in the midst of beautiful scenery, frequented not only on account of its baths but as well on account of its fine bracing air and attractive situation. There are numerous and interesting excursions in the environs, of both scenic and historic interest. Chatsworth and Haddon Hall, for example, are within easy access.

Like Bath, which it also resembles in its waters, Buxton was known to the Romans; was visited by Mary, Queen of Scots; and has, for a very long period, maintained a high rank as a prosperous and popular health resort and spa. Unlike Bath, however, Buxton is a summer resort principally, the season extending from May to September. The air is cool and invigorating. For July, during a period of ten years' observation, the mean maximum temperature was 65.1° F., and the mean minimum 48.4° F. There is considerable rain, the yearly mean being 46.2 inches.

The waters of Buxton are of the *simple thermal* variety, of a natural temperature of 82° F. They are very weakly mineralized, slightly alkaline, soft, and contain in solution nitrogen gas in larger amounts than is present in other springs of the kind. The color of the water is of a "beautiful blue tint." Besides the simple thermal waters, there is a weak chalybeate water used both for drinking and as an application to the eyes. Radium has also been found in these waters and it is possible that radioactivity may enhance their therapeutic value as well as that of other mineral waters where this rare element is found. These waters are employed both for drinking and baths. There is a handsome "pump room" for drinking the waters and two bath establishments, one in which the water is used at its natural temperature, and one in which the water is heated to any temperature desired. The usual varieties of baths are afforded here—douches, vapor, needle, and massage baths. There are also arrangements by which cripples are lowered into the waters.

The effects obtained by the use of thermal waters like those of Buxton are derived chiefly from their skilful application rather than from any mineral ingredients they possess, together with the careful ordering of one's habits of living in regard to diet, exercise, fresh air, and rest. Much of the benefit obtained by a visit to such spas as Buxton depends undoubtedly upon the change from one's usual routine of life and the pleasant surroundings of the spa.

The diseases and conditions which are benefited by the waters of Buxton are gout and gouty affections, rheumatism, diseases of the skin dependent upon a gouty diathesis. Joint stiffness and pain resulting from an attack of rheumatism are also relieved by the application of the hot water in the form of the douche massage, and the various baths which promote the absorption of morbid products and thus relieve the consequent disability.

The contraindications are: (*a*) febrile conditions; (*b*) advanced valvular disease of the heart, feeble or fatty heart, or atheromatous vessels; (*c*) advanced disease of the kidneys; (*d*) extreme debility; (*e*) advanced disease of the lungs; (*f*) plethora, or an inclination thereto.

The general action of the waters is said to be stimulating, alterative, depurant, and diuretic. Upon the skin they exercise a detergent effect, improving its tone and function. Excretion of urea and uric acid is said to be increased. In beginning a course of baths there may follow certain nervous or circulatory disturbances, such as insomnia, giddiness, palpitation, and sometimes slight fever with increased pain and stiffness in the joints, but these effects soon pass away.

The natural baths, *i.e.* at a temperature of 82°, are given from four to seven minutes, and the hot baths, those artificially heated, from four to fifteen minutes. After the bath the patient is wrapped in hot towels and dried by gentle rubbing. After the natural bath a brisk walk is recommended.

There are the usual means of amusement—theater, concert-hall, reading-room, tennis, golf, conservatories, etc. The accommodations are good, consisting of numerous hotels and boarding-houses.

Buxton is reached in four and one-half hours from London. EDWARD O. OTIS.

Byford, William H.—Born at Eaton, Ohio, March 20, 1817. He received the degree of Doctor of Medicine from the Ohio Medical College, in 1844, and began the regular practice of his profession at Mount Vernon, Indiana. (He had already practised there without a diploma during the preceding four years, in partnership with Dr. Hezekiah Holland.) During the ten years which he spent in Mount Vernon he won such a high position for himself in the esteem of the Profession of the State that he was called, in 1850, to fill the chair of Anatomy in the Evansville Medical College. Two years later he was transferred to the Chair of Theory and Practice in the same college and he continued to hold this position up to 1856, when the institution ceased to exist. Not long afterward he was made Professor of Obstetrics and Diseases of Women and Children in Rush Medical College, Chicago. In 1859, when the Chicago Medical College was organized, he resigned his chair in Rush Medical College and accepted a professorship in the newly established institution. In 1879, after he had been prominently connected with the Chicago Medical College for twenty years, he was again called to Rush College to take the Chair of Gynecology, a professorship which had been newly established, with the understanding that Byford would accept the position. Coincidently with his work in the medical school and his private practice, he found time for organizing the Women's Medical College of Chicago. He also was a prominent mover in the enterprise which gave to Chicago a medical periodical of character and standing—the *Chicago Medical Journal and Examiner*, —and for three years he was editor-in-chief of that publication. He died on May 21, 1890.

Of the writings which Byford published the following deserve special mention: "Chronic Inflammation of the Cervix Uteri"; "Treatise on the Chronic Inflammation and Displacements of the Uterus," 1864; "Practice of Medicine and Surgery Applied to Diseases of Women," 1865; and a "Treatise on the Theory and Practice of Obstetrics," 1870.

A. H. B.

Cabell, James Lawrence.—Born in Nelson County, Virginia, August 26, 1813. He studied medicine at the University of Maryland and received his degree in 1833. He continued his medical studies in Paris, France, and upon his return to this country he was elected (1837) Professor of Anatomy and Surgery in the University of Virginia. Soon afterward, however, he was given the Chair of Physiology and Surgery. In 1846 he was chosen Chairman of the Faculty. In 1875 he received the degree of LL.D. from Hampden-Sidney College. In 1878 he was elected President of the American Public Health Association, and afterward he held for a number of years the position of President of the National Board of Health. In 1847, in a paper which he read before the American Medical Association, he proposed that licences to practice medicine should be conferred, not by medical colleges, but by Boards of Medical Examiners altogether independent of medical schools. This plan has since been adopted in all the States. In 1887, at the close of fifty years' service as Professor in the University of Virginia, the alumni of that institution presented him with a handsome cup and desk as tokens of their appreciation. He died on August 13, 1889, and his remains rest in the University Cemetery.

Cabot, Arthur Tracy.—Born in Boston, Mass., in 1852. He received the degree of M. D. in 1876. He served as a surgical interne at the Massachusetts General Hospital, and then went abroad for further study, especially in the department of surgery. While in London he had the privilege of listening to Lister's inaugural address at King's College. Cabot was deeply impressed by what Lister said on the subject of the antiseptic treatment of wounds, and upon his return to the United States he became one of the most active advocates of this method. In 1886, Cabot was chosen a visiting surgeon to the Massachusetts General Hospital, and he held this position up to the year 1907. For a period of several years he was Surgeon to the Carney Hospital and also to the Children's Hospital. From 1885 to 1896, he held the position of Instructor in Genitourinary Surgery in the Harvard Medical School. One of the important contributions which he made to general surgery was a wire splint for fractures of the lower leg, an apparatus which he devised while he was connected with the Children's Hospital, and which is in large use throughout the world. It displaced the old fracture box. Although Cabot was an excellent general surgeon, possessing great manual skill and rare soundness of judgment, it was as a genitourinary surgeon that he became chiefly distinguished. In the later period of his professional career he devoted much time and thought to the campaign against tuberculosis, and he was appointed in 1907, by the Governor of the State, a trustee of the Massachusetts State Hospitals for Consumptives. About the year 1886, "realizing the importance of immediate pathological examination of many surgical cases while under operation in order to determine the scope and nature of the necessary operation," he and his brother Samuel established a fund of $10,000, known as the 'Samuel Cabot Fund for Pathological Research,' in memory of their father. The interest of this fund is used for paying a pathologist to be on hand operating days and making such examinations as the surgeons require. Dr. Cabot was helpful to the profession and also to the public at large in many other ways; but lack of space forbids any further mention of details in this brief sketch. He died November 4, 1912.

Dr. Cabot was a prolific writer; his contributions to medical literature numbering over one hundred and twenty papers. The following are the titles of a few of his more important writings: "A Contribution to the Treatment of Empyema," *Boston Med. and Surg. Journal*, August 16, 1883; "The Application of Antiseptic Principles to Genitourinary Surgery," *Op. cit.*, September 10, 1885; "The Choice of Operation for Stone in the Bladder," *Journal of the American Medical Association*, November 9, 1889; "Notes on the Non-operative Treatment of Enlarged Prostate," *Boston Med. and Surg. Jour.*, December 4, 1890; "Two Cases of Cholecystotomy," *Op. cit.*, April 28, 1892; "Observations upon Relapsing Appendicitis, with a Record of thirty-two Operations without a Death," *Op. cit.*, December 26, 1895; "Remarks upon the Proper Surgical Treatment of Tuberculous Bone Disease," *Op. cit.*, January 27, 1898; "A Case of Perforating Gastric Ulcer, Operation at the End of Twenty-four Hours," *Op. cit.*, August 11, 1898; "The State and its Part in the Tuberculosis Movement," State Memoir, September, 1908; and five articles, written in association with Dr. Hugh Cabot and published in the second edition of the REFERENCE HANDBOOK OF THE MEDICAL SCIENCES, upon the following topics: "Bladder in the Male," "Litholapaxy," "Lithotomy," "Suprapubic Cystotomy," and "Prostate Gland."

A. H. B.

Cacao, Butter of.—*Oleum Theobromatis. Oil of Theobroma. Cocoa Butter.* "A fixed oil expressed from the seeds of *Theobroma Cacao* L. (fam. *Sterculiaceæ*)." (U. S. P.) The chocolate tree is a native of tropical South America, where we have occasionally seen small forest areas which consisted almost wholly of it. These wild trees only occasionally produce fruit, for which the trees are very extensively cultivated in all tropical countries. There is great variation in the quality of the seeds coming from different regions. Under cultivation, the tree grows like an apple tree, which it closely resembles, from a distance, in form and general appearance. The oblong-ovate leaves are about a foot in length, thick, and rich looking. The flowers are small and inconspicuous, growing in little cymes directly from the bark of the branches, or even of the trunk. The fruit, about six to ten inches long and half as thick, is oblong-ovoid, coarsely ribbed or grooved, so as to look not unlike a narrow pointed melon. It has a thick, hardish rind, like a pumpkin or squash, and its color varies through shades of yellow, orange, and red to purple. It is filled with a whitish pulp, as soft as the flesh of a ripe melon and of a very fine texture. The numerous seeds are embedded in this pulp and attached to a soft central placenta. This pulp forms the basis of a delicious jelly of a beautiful purple or wine color. The seeds, after being cleaned of the pulp, are known as raw seeds. In this condition they are bitter and astringent and unfit for use. Two methods of curing are in vogue. The first is to enclose them in tight boxes and allow them to "sweat." The second is to "clay" them by burying in holes in the earth. Either process results in fermentation, by which the outer coating is caused to peel off, and they lose their disagreeable taste. They are then dried, cleaned, and marketed under the name "cacao" (pronounced (kah-kah'-o; or in English, kay-kay'-o). Venezuelan clayed cacao is probably the most highly esteemed and is the most expensive. The seeds are about as large as unshelled almonds, oblong-ovoid and somewhat flattened, blunt at both ends, of some shade of brown, veiny on the outer surface. The shell is thin and brittle, the cotyledons friable and fatty. The latter are wrinkled, and in good seeds fill the cavity loosely, with an irregular, small space in the center. The taste is slightly bitterish, but agreeable. For chocolate manufacture, the seeds are roasted and shelled and the kernels finely ground into a paste, with or (usually) without a very slight addition of water. In the process a portion of the oil separates. In the earlier manufacture in the United States, this, with frequently an additional portion, was removed, making our chocolate dry. We have since learned so well from our tropical relatives that we not only retain all of this oil, but abstract a portion in making the poorer grades of chocolate, to add to the richer and finer grades.

The seeds yield almost half their weight of fat, about a third as much albuminous matter, considerable starch, and about one and one-half per cent. of the alkaloid *theobromine*. The shells removed from the seeds yield about one per cent. of this alkaloid. They are utilized for the preparation of an inferior drink. The use of chocolate produces, in a milder degree and after a longer time, the cerebral stimulation of coffee. As the latter acts through its caffeine, which is methyl theobromine, it would appear that some transformation of the theobromine of chocolate must occur in the system.

Cacao butter is obtained from the seeds by the aid of heat, either by pressing with heated rollers or by boiling. The cake which remains is ground into "breakfast cocoa." The shells yield a very small amount of the fat, which is occasionally seen in the market as "cocoa-shell butter." Cacao butter occurs in cakes of a yellowish-white color; has a slight, agreeable odor and an oily taste, a little like that of chocolate. Its specific gravity is from 0.970 to 0.980. It melts at from 86° to 91.4° F., and is soluble in 100 parts of alcohol. It is much subject to adul-

teration with other fats, for the detection of which the Pharmacopœia provides ample tests. The peculiarities of this fat are its hardness and its melting point, at about the temperature of the body. This combination renders it exceptionally useful for the making of suppositories and bougies. As it does not readily decompose like other fats, it becomes a useful base for medicaments, and is, for the same reason, frequently employed in hot countries as a delicious substitute for butter. It has no distinctly medicinal action. HENRY H. RUSBY.

Cachexia.—This word is derived from the Greek, κακός, bad, + ἕξις, a habit of body. The condition is characterized by a general lack of nutrition, with wasting, occurring in the course of a chronic disease. Among the well-recognized *varieties* are African or negro cachexia, earth-eating cachexia; cachexia aphthosa, or sprue; cachexia aquosa, an edematous form of uncinariasis; cachexia hypophyseopriva, following total removal of the hypophysis cerebri; cachexia strumipriva or thyreopriva; cachexia thyroidea, pachydermic cachexia, myxedema; lymphatic cachexia, Hodgkin's disease; malarial cachexia; mercurial cachexia; saturnine cachexia, due to chronic lead poisoning; splenic cachexia, a pernicious anemia with enlargement of the spleen; urinary cachexia, accompanying suppuration along the urinary tract; cancerous cachexia; miner's cachexia, dochmiasis; and thyroid cachexia, exophthalmic goiter.

CLASSIFICATION.—A classification based upon etiology is the most satisfactory. The following is practical and simple:

1. Cachexia due to chronic infection: (*a*) Dochmiasis; (*b*) Uncinariasis; (*c*) malarial cachexia; (*d*) cachexia aphthosa (thrush). (*e*) septic cachexia, *e.g.* urinary cachexia; (*f*) cancerous cachexia; (*g*) syphilitic cachexia.
2. Cachexia due to alterations of the internal secretions: (*a*) Myxedema; (*b*) strumipriva, or thyreopriva; (*c*) hypophyseopriva; (*d*) exophthalmic goiter; (*e*) lymphatic cachexia; (*f*) splenic cachexia.
3. Toxic cachexia: (*a*) Mercurial cachexia; (*b*) saturnine cachexia; (*c*) arsenical cachexia.
4. Cachexia due to hemorrhage, or wasting discharges.
5. Cachexia due to improper food, *e.g.* scurvy, pellagra.

ETIOLOGY.—The more prominent causes of cachexia are malaria, syphilis, chronic sepsis, phthisis, lead poisoning, cancer, and infantile scurvy. Cachexia strumipriva, due to destruction or removal of the thyroid gland, is easily recognized. Cachexia may be due to hemorrhage from the nose, lungs, gastrointestinal tract (in association with the *Ankylostoma duodenale*, ulcer, cancer, hemorrhoids), the female genital tract, the bladder, and in the various forms of hemorrhagic diathesis. Insufficient nourishment and bad hygienic conditions are often etiological factors. Malignant tumors, severe organic disease, poisons, and parasites may be factors in causing cachexia. Spermatorrhea, lactorrhea, catarrh of the respiratory and alimentary tracts, are supposed to be causes. The rôle played by albuminuria and fever is rather to be ascribed to the diseases causing these conditions. The animal parasites produce cachexia through the elaboration of toxins. Among the mineral poisons, lead, mercury, and arsenic are the chief causes of cachexia. Cachexia, like anemia, may be caused by syphilis. The diagnosis of syphilis in such cases must depend upon concomitant symptoms, the Wassermann reaction, and especially the therapeutic test. It should be remembered that a syphilitic may have a cachexia due to some other cause, in which case the syphilis usually adds to the gravity of the prognosis. In syphilitic cachexia, other evidences of syphilis usually abound, relics of existing or preëxisting stages of the disease.

DIAGNOSIS.—Cachexia is a symptom and should not be accepted as a satisfactory diagnosis in any case Most important is the recognition of the cause of the cachexia. The color and general appearance of the cachectic individual are too well known to merit description.

Cachexia is one of the cardinal symptoms of malignant diseases. Incidentally, the diagnosis of such affections should be made before the appearance of cachexia, notwithstanding the comparatively early development of cachexia in the cancers.

The cachexia of syphilis improves under antisyphilitic treatment, *e.g.* with the iodides, which cause no improvement of the cachexia of tuberculosis, or actually make it worse.

PROGNOSIS.—The outlook depends upon the cause, and upon the degree of marasmus in those cases in which the cause of the cachexia can be removed. In any case, the occurrence of cachexia adds gravity to the prognosis. On the other hand, it is doubtful if we are ever justified in robbing the patient of all hope, for recovery has occurred even in some apparently far advanced cases of malignant disease with marked cachexia.

TREATMENT.—The treatment is the treatment of the underlying condition. The cause must be removed, if possible.

Among the host of remedies that have been used in the treatment of cachexia, iron, arsenic, and strychnine deserve more than passing notice. Iron in the form of the green citrate, came into use first among the Italians in the treatment of the severe cachexia of malaria, the remedy being administered hypodermatically. For this purpose the dosage is usually about gr. jss (0.1) for the adult, the iron being given alone or combined with arsenic, or strychnine, or both. The injections are made deep, preferably into the muscles of the thigh.

Arsenic is a very old remedy. The forms commonly used are Fowler's solution, the Asiatic pill, Roncegno water, the arsenate of sodium, and cacodylic acid and the cacodylates. The form used depends largely upon the idiosyncrasies of the patient and the preference of the physician. Usually the best results are secured by pushing the remedy to the point of tolerance.

Iodine and the iodides are of especial value in syphilitic cachexia. The iodide of potassium is the form usually employed. Sometimes the iodide of sodium is better tolerated. In severe cases I have sometimes apparently secured better results by the deep subcutaneous injections of iodipin, a solution of iodine in sesame oil. The iodine preparations should not be used in the cachexia of phthisis.

In the cachexiæ due to defective internal secretions, we may attempt to supplant the defective secretion. Thus, good results are secured in cachexia strumipriva by the use of the thyroid gland or preparations of it, such as the desiccated gland or dry extract, thyroiodin, thyraden, Fränkel's thyroantitoxin, thyrogen, thyroglandin. My experience has been chiefly with the thyroid extract and thyroiodin, which have proven very satisfactory. Of these the initial dose of from two to five grains (0.13–0.5) should be gradually increased, keeping well within the tolerance of the patient.

In severe, intractable cases of malarial cachexia, good results have sometimes been reported after removal of the spleen. The operation is dangerous and seldom justifiable.

Most important are the knowledge and proper treatment of the cause of the cachexia, combined with suitable food and tonic treatment, and good hygienic surroundings.

It will be noted that we have not mentioned "idiopathic" cachexia. We would not encourage the use of this term, since it tends to stultify the search for the cause. Strictly speaking, there are no idiopathic diseases or symptoms. The use of the term may ease the conscience, but it is without any real meaning to the scientific physician, save that it indicates that the one using it has been too indolent to find the cause.

GEORGE E. MALSBARY.

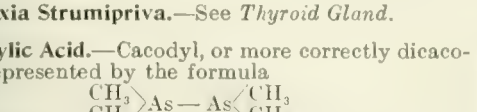
Cachexia Hypophyseopriva.—See *Hypophysis Cerebri.*

Cachexia Strumipriva.—See *Thyroid Gland.*

Cacodylic Acid.—Cacodyl, or more correctly dicacodyl, is represented by the formula

$$(CH_3)_2As-As(CH_3)_2$$

Cacodylic acid is arsenic acid in which two hydroxyl groups have been replaced by two methyl groups:



Arsenic Acid — Cacodylic Acid

Cacodylic acid is comparatively inert and harmless: it imparts an alliaceous odor to the breath, but in therapeutics it is generally replaced by one of its salts, chiefly sodium cacodylate.

Sodium Cacodylate has been recommended in most cases where arsenic is employed; it has been used in various skin diseases, anemia, chlorosis, diabetes, malarial cachexia, phthisis, and in syphilis. The dose is one-half to two grains (0.03–0.13) and the drug may be administered hypodermically or in pills. Sodium cacodylate is soluble in an equal amount of alcohol, and in half the amount of water.

Cacodylates of iron, of magnesium, of guaiacol, and of strychnine have been employed; but the whole class of aliphatic arsenic compounds has but little therapeutic importance, and has been practically superseded by the aromatic compounds of arsenic.

R. J. E. SCOTT.

Cactaceæ.—(The Cactus family.) This strange and interesting family of plants occupies as yet a most uncertain place in the materia medica. It comprises some twenty genera and probably six hundred species, and its study is no less difficult for the botanist than for the pharmacologist. The plants grow chiefly in desert regions, being competent to withstand the most extreme conditions of aridity, and interest centers chiefly in their defensive provisions. The absence of leaves, which are usually metamorphosed into spines, protects them against desiccation. The succulent nature of their stems causes them to be sought by hungry and thirsty animals. In times of cattle famine, the spines are burned off and the stems then used as fodder, while a wholesome water supply can be obtained from cavities scooped out in the bodies of some of the thicker species. Against destruction from such causes, most of them are protected by their armament of spines. Those which lack this armature are commonly protected by poisonous alkaloids, and attempts have been made to utilize some of these in medicine. Spineless varieties are now being developed by plant breeders for use as stock food. The important drugs of the family are the *Cactus grandiflorus* and the *Mezcal Buttons*, which see.

Their physiological properties are diversified. The berry-like fruits are commonly edible, and some of them, like the prickly pear or tunya, are of much economic importance. Several of them are hosts for the valuable cochineal insect. Many succulent plants not related to this family are popularly called cactuses.

HENRY H. RUSBY.

Cactus Grandiflorus. CEREUS GRANDIFLORUS. The flowers of *Cereus grandiflorus* (L.) Miller (fam. *Cactaceæ*). The stems have also been used. This plant, the well-known Night-blooming Cereus of cultivation, is a native of the West Indies, and flowers in August. Adulteration with, or substitution by, the flowers of *Opuntia decumana* Haw, as well as by *C. macdonaldiæ* Hooker, the Night-blooming Cereus of Mexico, is very extensive. The flowers of *O. decumana* are cup-shaped, about an inch long and broad, with stamens one-fourth or one-half of an inch in length; while the genuine flowers are eight to ten inches in diameter when fully spread out, and have stamens two or more inches long. Much of the contradictory testimony as to composition and properties is doubtless due to this irregularity in the drug used, yet there is a wide discrepancy of opinion as to the merits of that which is genuine. No efforts appear to have been made to compare the flowers collected in different stages of maturity. The facts here stated, however, appear to be fairly well established. Both the stems and the flowers appear to be active, but the latter more so. An alkaloid and a glucoside are claimed, but our information regarding them is very meager and indefinite. The drug is a cardiac stimulant of peculiar action. It does not affect the stomach nor the centers as digitalis does. It increases blood pressure by quickening and strengthening the heart beat, through direct action upon its nerves. Wilcox, who has studied it extensively, is positive in asserting its value in aortic regurgitation, where digitalis cannot be used, but its injuriousness in mitral stenosis. He recommends it generally in relative cardiac incompetency and functional cardiac weakness. The dose of the fluid extract is (♏x. to xxx.) (0.6–2.0).

HENRY H. RUSBY.

Cadaverine, $CH_2.CH_2.CH_2.CH_2.CH_2$ (NH$_2$ and NH$_2$) (pentamethylendiamine), one of the diamines found in decomposing protein, in intestinal putrefaction, and sometimes in the urine of cystinuric individuals. It possesses only slight toxicity. See *Ptomaines.*

FRANK P. UNDERHILL.

Cade, Oil of.—OLEUM CADINUM. *Oleum Juniperi Empyreumaticum.* "A product of the dry distillation of the wood of *Juniperus oxycedrus* L. (fam. *Coniferæ*)." (U. S. P.) The British Pharmacopœia includes "some other species" in the source.

J. oxycedrus resembles in general the common juniper of Europe, but has larger, reddish-brown, shining fruits (1.25 cm. in diameter—0.5 in.) It is an inhabitant of the Mediterranean basin, growing in waste places and upon stony hillsides.

Its tar has been used for centuries by the peasants of southern France for the "sheep itch" and other cutaneous affections of their cattle, but its employment in medicine, although occasional and also of old date, has been extensive only since its recommendation by the German school of dermatologists in the treatment of eczemas. It is prepared by a method similar to that used in the manufacture of ordinary tar; that is, by distillation *per descensum*, in rude stills or ovens, from the bottom of which it is collected and then sold without further purification. The principal center of its production is Nîmes.

It is a thin tar, often black in mass, but brown or brownish yellow and transparent, in thin layers; and is more fragrant and pleasant in odor than common wood tar, which it otherwise resembles. The taste is acrid and empyreumatic. Its composition is not notably different from that of the tars of other conifers. *Cadinene* ($C_{15}H_{24}$) is its important odorous constituent. The principal use to which it is put in medicine is that

mentioned above—for the local treatment of eczema in the scaly stage. It is also used in other chronic inflammatory and exfoliating skin diseases. It may be applied by rubbing in with the fingers or a cloth, or, what is better, with a stiff-haired brush. If desirable to dilute it, some bland oil may be mixed with it, or it may be made into an ointment with lard or tallow, or with vaseline. Soaps containing it are also considerably used. Stockings, gloves, and bandages saturated with it are sometimes worn. Besides its stimulating properties, oil of cade is a good parasiticide, an efficient antiseptic, and a local anesthetic—properties which it undoubtedly owes to the creosote and similar substances which it contains. It is never used internally.

W. P. Bolles.

Cadmium.—Cadmium is a white metal which resembles zinc in both its physical and chemical properties. Symbol, Cd; atomic weight, 112.4. *Cadmium Sulphate* is the only salt of this metal that merits notice in medicinal relation. It was official in the United States Pharmacopœia of 1870, and, though dropped in the revision of 1880, it is still employed. The salt, formula $CdSO_4,4H_2O$, occurs in small colorless, rhomboidal crystals, efflorescent on exposure. It is freely soluble in water, and has a subacid and astringent and metallic taste. In properties it most closely resembles zinc sulphate, being an irritant astringent. Taken internally, it will determine vomiting, after the manner of zinc sulphate, and in overdose will prove poisonous. Its claim for recognition in medicine rests on an alleged peculiar potency in determining the absorption of such corneal opacities as are capable of undergoing that process—a potency certainly not much, if at all, greater than that possessed by the commoner salts, silver nitrate or zinc sulphate.

Cadmium sulphate is generally used in solution of from one-half to one per-cent. strength.

Toxicology.—Cadmium and its salts are unimportant from a medico-legal point of view. Their uses are limited, and they are seldom met with outside of the chemical laboratory. The metal is employed occasionally in alloys to reduce their fusing point, and an amalgam has been used by dentists for filling teeth. The most important compounds are the iodide and bromide, which are used in photography for iodizing and bromizing collodion. The sulphate of cadmium has been used externally, as an astringent and stimulant, in the treatment of conjunctivitis and ulcers and opacities of the cornea. The iodide of cadmium, in the form of an ointment, has been recommended for external use, particularly in the treatment of scrofulous enlargement of the glands. The sulphide of cadmium has been used, to a limited extent, as a yellow pigment. Excepting the sulphide, the compounds mentioned are colorless, soluble in water, and possess a disagreeable metallic taste.

Symptoms.—Preparations of cadmium have given rise, occasionally, to accidental poisoning. They appear to act as irritants, resembling in general the salts of zinc. Vomiting, diarrhea, vertigo, labored respiration, loss of strength, and cramps followed the inhalation of the dust arising from a polishing powder containing carbonate of cadmium (Sovet). Two ladies took an uncertain but small dose of bromide of cadmium by mistake for bromide of ammonium. It caused severe pain and a burning sensation in the stomach, accompanied by vomiting and purging which lasted for five hours. During a part of this time the pulse was imperceptible. There were no cerebral symptoms. Both patients were confined to their beds for several days, during which time their stomachs continued irritable (Wheeler). At the date of publication of the previous edition of this work, Hills was able to find only one fatal case of cadmium poisoning recorded. The patient, a lad fourteen years of age, took an unknown but probably large dose of chloride of cadmium, which had been sold for Epsom salts. It caused immediate vomiting. On admission to the hospital a short time after, he was in a state of collapse, with cold, clammy skin; radial pulse scarcely perceptible; respiration feeble, slow, and sighing. There was no stertor. The mucous membrane of the mouth was pale and sodden, the tongue greatly swollen. He was apparently unconscious, though when shaken and aroused by dashing cold water upon the face, he replied rationally, in a hoarse whisper, to any questions put to him. There was extreme restlessness. Deglutition was impeded. Death took place in about an hour and a half after the ingestion of the poison. At the post-mortem examination the vessels of the brain were found filled with blood; the left lung was congested (*Indian Medical Gazette*, Calcutta, 1866, i., 156).

Treatment.—This should be much the same as in cases of poisoning by salts of zinc. Vomiting should be assisted, if necessary, by the free administration of warm water, with milk or mucilaginous liquids; or the stomach may be emptied by means of the stomach tube. The subsequent irritation may be allayed by the use of opium. Marmé recommends, in cases of acute poisoning, the alkaline carbonates with white of eggs.

Edward Curtis.
R. J. E. Scott.

Caffeine.—*Theine*, $C_8H_{10}N_4O_2,H_2O$. "A feebly basic, proximate principle, obtained from the dried leaves of *Thea sinensis*, Linn. (fam. *Ternstræmiaceæ*), or from the dried seeds of *Coffea arabica*, Linn. (fam. *Rubiaceæ*), found also in other plants." (U. S. P.)

It occurs in fleecy masses of long, flexible, white crystals, permanent on exposure, of a silky luster, having a bitter taste, and without odor. Soluble in eighty parts of cold water, in two parts of boiling water and in thirty-three parts of alcohol. It is neutral to test paper. When ignited it is consumed without residue. A notable feature is the unusually large proportion of nitrogen that it contains.

The only official preparation is the so-called citrate (caffeina citrata) which is very unstable and rapidly deteriorates, the alkaloid separating and remaining uncombined. When mixed with three parts of water, the citrate forms a thick liquid; when more water is gradually added the caffeine is precipitated, but redissolves and forms a clear solution when twenty-four parts of water are added. It is a white powder, without odor; it has a bitter taste and an acid reaction. When burned it chars and leaves a slight ash. It is soluble in thirty-two parts of water.

An effervescing citrate is official in the United States Pharmacopœia and the British Pharmacopœia. The former contains one per cent. of caffeine, that of the British Pharmacopœia contains nearly four per cent.

Caffeine is the characteristic alkaloid of coffee and tea. It was discovered and first prepared, in an impure condition, from coffee, by Runge, in 1820, and shortly after, in a state of greater purity, by Pelletier and Robiquet, and other chemists. In 1827 Oudry separated an alkaloid from tea, which he named *theine*. This, in 1838, was proved by Mulder and C. Jobst to be the same as Runge's caffeine. In 1840 Martius discovered *guaranine* in guarana, and afterward the same observer, and others, proved its identity with the alkaloid of coffee. The same substance was also found, in 1843, by Stenhouse, in the leaves of maté or Paraguay tea, and in 1865, by D. Daniel and by J. Attfield, in the kola nuts (*Sterculia*) of Africa. In all these products it appears, moreover, to be the most important ingredient. As no two of these plants are nearly related to each other, or are even in the

ame order, caffeine may yet be found to be as widely distributed in the vegetable kingdom as berberine or oxine. It is an interesting fact that all the above substances have been used from a remote time by communities which could have had no communication with each other, for exactly the same purpose, iz., as a stimulating and comforting addition to their daily food; tea by the Chinese, coffee by the Arabs, he kola nuts by the Africans, and maté and guarana y different tribes of South America.

For commercial purposes caffeine is prepared exclusively from tea and coffee; the poorer sorts, that is "tea dust" and damaged and inferior grades of either tea or coffee, being used. As the price of both these articles does not depend at all upon their alkaloidal strength, but only upon their appearance and flavor, the cheaper grades often contain considerably more caffeine than the more expensive ones, and, price apart, are better for this purpose.

The percentage of the alkaloid in the several plants varies greatly. It is estimated that tea contains from one to four per cent.; coffee, one to three; maté, one to two; and guarana about five per cent.

Caffeine acts upon the cerebral, medullary, and spinal centers, primarily as a stimulant and later as a depressant. Its action is also directed to the muscular tissue, improving its tone and contractile power, until ultimately it merges into the general depression.

In small doses, from one to three grains, it produces a sense of well-being, and a feeling of increased strength and vigor. The cerebral functions become more active, the respirations are deeper, the heart beats more forcibly, and the arterial tension is increased. The heart at first participates in the general stimulation, and there is an increase in the frequency of the pulse, but this is transitory, as the inhibitory centers are soon influenced by the stimulation and produce a slowing of the heart's action, which, with the more forcible contraction of the muscular walls, constitutes its most desirable effect. The urine is increased, both the quantity and the contained solids being greater. Tissue change is accelerated, and the body temperature rises. This beneficial action continues for some days, after which the continued use is liable to give rise to signs of cardiac irritation and excessive vascular tension. There may be a rapid, hard pulse, a feeling of constriction in the chest, dyspnea, and labored action of the heart.

In larger doses, from gr. v. to gr. viij. or x., the symptoms of overstimulation are developed early, and if the drug is continued, the depression follows rapidly and may become very marked. In addition to the cardiac and respiratory distress, there are insomnia, vertigo, tinnitus aurium, flashes of light, mental distress, and delirium. As the depressant action replaces the stimulation, the inhibitory control of the heart is lost and there follows a rapid, feeble heart beat, which gradually increases until contractions cease. The respirations also become shallow, and there follows a condition of asphyxia and collapse, death being due to respiratory failure. Caffeine is an irritant to the gastric mucous membrane, and its continued use produces heat and burning at the epigastrium, with nausea, which may terminate in pain and severe irritation of the stomach and intestines.

Caffeine was formerly considered only as a cardiac stimulant and administered freely, with very little thought of any subsequent depression. Later experience has shown that this secondary action is of the greatest importance, and although often unrecognized, it is a frequent cause of serious depression, and possibly of death. Cases of acute poisoning are rare, and in healthy adults the quantity necessary to cause death would be very great, but in diseased states its action is much accentuated. In valvular disease and in conditions in which the heart is being overtaxed, even ordinary doses may be attended by very serious consequences. The danger is not only from large doses, but also from the continued use of moderate doses.

Attention has also been directed to an unfavorable condition that may arise during its administration, prior to any depressant action. This is an overstimulation and irritation of the cardiac ganglia that may terminate in a spasmodic contraction of the heart and death. The following are given as instances of death from this cause. In a case of pneumonia, death occurred suddenly, when the patient was taking caffeine, three grains three times a day. A woman with chronic parenchymatous nephritis, anasarca, and double pleural effusion had taken small doses for some time previous to a sudden fatal syncope. In a third case death took place suddenly, the patient being a young girl who had acquired the habit of taking frequent doses of gr. iv or v. (0.25–0.3). In all these cases a postmortem examination was made and the heart found firmly contracted, death being due to a condition described as a "tetanus of the heart muscle."

Caffeine is employed as a cardiac and general stimulant, as a diuretic, and for the relief of headaches and neuralgia pains. Its value as a stimulant is well recognized, and its rapid action makes it of value in cases of sudden weakness and threatened syncope. In addition to its value in threatened heart failure, it is most useful in chronic valvular disease, to counteract a failing compensation. It, however, must always be given cautiously when the heart is feeble and dilated, or in any form of heart disease in which the walls are diseased. In arteriosclerosis it is also contraindicated, as it adds to the already high arterial tension.

The diuretic action of caffeine is always to be depended upon, and is that for which it proves of greatest service. It is in a measure due to the increased arterial pressure, but caffeine also exercises a direct action upon the renal secreting tissue. It is particularly indicated in the dropsy of cardiac disease, and resembles digitalis in its action. It acts more rapidly, but has not the same power to strengthen the heart and increase the blood pressure. For this reason its effects are often better when preceded by digitalis, or when the two are combined. When there is kidney disease it must be given with care, as the stimulation of the renal tissue may aggravate the local trouble. In dropsy due to hepatic disease, its action is very uncertain.

Caffeine has not proved of much value in the treatment of headaches. In many forms of neuralgia and migraine, in the debilitated and nervous, it may prove of service, but this is due to the improved tone of the nervous system, and not to any anodyne or analgesic property.

In administering caffeine, the citrated form (*Caffeina Citrata*, U. S. P.) is frequently selected on account of its greater solubility. When used it should have been carefully preserved, and it must be given in powder, or dissolved immediately before use, as it rapidly decomposes when in solution. Citrated caffeine is one-half the strength of the pure alkaloid, and gr. x.–xv. (0.6–1.0) during the day is the average dose. Of this we have an effervescent form (*Caffeina Citrata Effervescens*, U. S. P.), the strength of which is four per cent. When an immediate effect is required, it may be administered subcutaneously. A product that is much employed is the double salt of caffeine, with soda and salicylic, benzoic, or cinnamic acid. It is very soluble and unirritating, and furnishes the best solution for hypodermic use. It is about one-half the strength of the citrate. These salts were proposed as the best means of obtaining the diuretic action of caffeine, but later experiments seem to indicate that these combinations are not so serviceable as were expected. It has been found that the presence of soda and salicylic acid has a tendency to reduce blood pressure and to lessen the secretion of urine. This, it is thought, must influence unfavorably the caffeine

when it is thus combined with other drugs. The compound salts, however, are frequently employed. The following formulæ for their preparation are official in the Paris Codex: (1) Caffeine, 4; sodium salicylate, 3; distilled water to 10 parts. (2) Caffeine, 2.5; sodium benzoate, 3; distilled water to 10 parts.

BEAUMONT SMALL.

Caisson Disease.—*Synonyms:* Compressed-air illness, diver's palsy.

Among the occupational diseases, caisson disease, better termed compressed-air illness, holds an important place. It has been widely discussed on account of its obscure and complicated etiology, its varied symptoms, its treatment, and its unfortunately frequent termination in death or permanent disability. The recent demands of modern engineering for the use of compressed-air chambers in the construction of foundations for bridges and large buildings and in subaqueous tunnelling, have made cases of compressed-air illness common within the past decade. The prevalence of cases of compressed-air illness in large undertakings where compressed air is used is shown by the fact that in a period of about twenty-eight months, during the work on the four Pennsylvania East River tunnels in New York City, 3,692 cases were treated in the emergency hospital connected with the work. During this time, approximately 1,000 men were working daily in pressures varying from fifteen to forty-two pounds +. No doubt many mild cases occurred which did not apply for treatment and were not included in this number. Most of the cases treated were simple cases of pain in the extremities, but 144 of them might be classed as serious cases, and twenty were fatal. The percentages of illness and of serious cases were probably no greater than might be expected in any compressed-air work under similar conditions.

HISTORY.—The earliest mention of compressed-air illness was made by Triger, a French engineer, who designed the first practical caisson in 1839. He called attention to the occurrence of pains in the extremities of the workmen employed. LeRoy de Méricourt, in 1868, published the first medical report of compressed-air illness among sponge divers. Since these reports many contributions to the subject of compressed-air illness have been made. Writers upon the subject, most worthy of mention, are Pol and Wattelle, Paul Bert, Heller, Mager and von Schrötter, Leonard Hill and associates, and J. S. Haldane and associates.

ETIOLOGY.—Of the various theories that have been advanced to explain the symptoms arising from the effects of compressed air, two may be mentioned as of importance. These are: (1) The mechanical congestion theory, (2) the gas emboli theory.

The Mechanical Congestion Theory.—This theory was first advocated by Pol and Wattelle in 1854, and at the time received general credence. It found its chief advocate in this country in A. H. Smith, who had charge of the medical work in connection with the construction of the Brooklyn Bridge. Smith stated the theory as follows: "My own opinion is that the long-continued pressure produces changes in the distribution of the blood, especially in the closed cavities, such as that of the skull and of the spinal cord. The greater the pressure and the longer it continues, the more decided will be these changes, and the less readily will the vessels resume their natural conditions when the pressure is relieved. Hence, if the pressure be suddenly reduced, congestion or blood stases result, particularly in the brain and cord, and perhaps also in the cavities of the long bones, which are often the seat of exquisite suffering."

Against this theory is the fact that symptoms of compressed-air illness never develop under pressure. Furthermore living tissue is a colloidal substance, containing about eighty per cent. of water, and is practically incompressible. Several observers have failed to find any appreciable change from normal in the peripheral circulation or in the blood pressure of men under increased atmospheric pressure. Hill watched the circulation in the web of a frog while under pressure as high as twenty atmospheres, and could detect no change in it. Autopsy findings, in which the presence of free gas in the circulatory system is one of the most frequent and characteristic features, cannot be accounted for by this theory.

The Gas-emboli Theory.—Paul Bert, in 1878, advanced this theory supporting it by logical reasoning and by experiment, and it is now almost universally accepted. Briefly stated this theory is as follows: The blood of a man or animal when in compressed air takes into solution an increased quantity of oxygen and nitrogen from the air, the quantity of the gases absorbed being in direct proportion to the increase of pressure. The gases taken up by the blood are gradually distributed to the fluids of the various tissues. With rapid decompression the nitrogen gas bubbles off in the blood. These bubbles act as emboli and block up the capillaries in one or another part of the body, and by cutting off the blood supply or by direct mechanical violence, cause the various symptoms of compressed-air illness. The increased solubility of gases under pressure and the saturation of the body fluids are in accordance with Dalton's law. The symptoms of illness may be prevented by making decompression slow enough to allow the absorbed nitrogen to escape from the lungs.

This theory depends upon physical laws, has been demonstrated to be correct by many experiments on animals by different observers, and has been conclusively proven by autopsies in many fatal cases of compressed-air illness.

From this theory as well as from practical experience the chief etiological factors have been deduced as follows:

The Degree of Pressure.—In general, the higher the pressure the greater the chances of compressed-air illness. It has been found that cases of illness seldom happen with pressures up to fifteen pounds +. Serious and fatal cases seldom occur with pressures below thirty pounds +. With pressures in the neighborhood of thirty pounds + one may expect cases of illness, which increase both in frequency and in severity as the pressures become higher.

Time under Pressure.—Up to a certain point (full saturation of the body fluids), the longer the time under pressure the greater the chances of compressed-air illness. Persons who spend but a few minutes in compressed air, even at high pressure, seldom if ever experience any symptoms after decompression. The nearer the time spent under pressure approaches the time necessary for complete saturation of the body fluids, the more likely are symptoms to develop. What this time is, is not definitely known. No doubt it varies in different individuals, and under different conditions. Some parts of the body saturate quickly, others slowly, depending on the blood supply of the various tissues. Fat not only saturates slowly, but has the property of taking up about six times as much nitrogen as blood. Bodily exercise and work hasten the time of body saturation. It is probable that it takes about two hours for one working in compressed air to attain approximately full body saturation. This question has an important bearing upon the arrangement of working shifts in compressed-air work.

Time Taken for Decompression.—The more rapid the decompression the greater the chances of compressed-air illness. During decompression, desaturation of the body fluids takes place; the fluids of the various tissues giving up their absorbed gases to the blood, the blood, in turn, giving them up through the lungs to the air. A considerable quantity of absorbed

gas is probably also eliminated through the intestinal wall and expelled as flatus. The time of desaturation, as in the case of saturation, varies in different parts of the body and in different individuals. Tissues which saturate slowly, desaturate slowly. Work and exercise during decompression hasten desaturation. Hill advocates the breathing of oxygen during decompression to hasten the elimination of nitrogen gas.

Just what is the shortest safe time for decompression from any given pressure has never been determined. Bert concluded that all trouble could be avoided by allowing thirty minutes for decompression from pressures between two and three atmospheres +, and sixty minutes for pressures of from three to four atmospheres +. Von Schrötter considered twenty minutes per atmosphere a safe time. Practical experience has shown that one may decompress from pressures up to fifteen pounds +, in one or two minutes, even after exposures of several hours, with comparative safety. Many men seem able to decompress rapidly from pressures of thirty pounds +, or even more, after long exposures, with impunity. At the Pennsylvania East River tunnels a rate of decompression was employed allowing one minute for each two pounds of pressure (fourteen minutes for twenty-eight pounds +, sixteen minutes for thirty-two pounds +). That this rate of decompression cannot be considered safe is shown by the fact that there were serious and fatal cases. The rate of decompression now required by the New York State law is two minutes for each three pounds of pressure up to thirty-six pounds +, and one minute for each pound of pressure when pressures above thirty-six pounds + are being used. It is not likely that this would prevent all serious and fatal cases in a work of the magnitude of the Pennsylvania East River tunnels.

Haldane proposed the interrupted or stage method of decompression. Starting from the fact that rapid decompression from nineteen pounds +, to normal atmospheric pressure is comparatively safe, he argued that it would be correspondingly safe to decompress rapidly from four to two atmospheres, or from six to three atmospheres; and he found this to be true in a series of experiments with animals. He proposed the following rate of decompression for caisson and tunnel work:

Rate of Decompression in Caisson and Tunnel Work.

Working pressure in pounds per square inch.	Number of minutes for each pound of decompression after the first rapid stage		
	After first three hours' exposure.	After second or third three hours' exposure, showing an interval for a meal.	After six hours or more of continuous exposure.
18–20	2	3	5
21–24	3	5	7
25–29	5	7	8
30–34	6	7	9
35–39	7	8	9
40–45	7	8	9

Table copied from "The Hygiene of Work in Compressed Air," Haldane, *Journal of the Society of Arts*, vol. xvi., Jan., 1908.

His first rapid stage of decompression reduces the pressure in about three minutes to a point equal to one-half the actual pressure. To illustrate—if the working pressure is forty pounds +, the actual pressure equals fifty-five pounds. One-half the actual pressure is 27.5 pounds, or 12.5 pounds gage pressure. Applying this table to decompression from forty pounds +, one would reduce the pressure in about three minutes to 12.5 pounds +, and then allow 87.5 minutes for the remaining decompression after the first three hours' exposure.

Bornstein compared the effects of stage and uniform methods of decompression at the Elbe Tunnel Works, Hamburg, where pressures of thirty pounds + were being used. The percentage of illness on the basis of man-shifts for the stage method was 0.15; and for the uniform method 0.19, a slight advantage for stage decompression.

Besides these three chief etiological factors, many others which might be called predisposing causes must be considered, chief among which are the following:

Age.—Boys, on account of underdevelopment, and men past forty are generally acknowledged to be bad subjects for compressed-air work.

Build.—Fat individuals are bad risks in compressed-air work and this should be avoided by them.

Organic Disease.—Persons with organic disease should not be subjected to work in compressed air because, even if they are not more susceptible to compressed-air illness, they are certainly less able than those with normal organs to stand the effects of such illness. Conditions of the nose, throat, or ears which prevent the equalization of pressure within the middle ear incapacitate workers in compressed air.

Alcoholism.—Alcoholics are bad risks for the same reason that those with organic disease are bad risks.

Newness to Work.—"Green" men are more likely to have symptoms of compressed-air illness than old workmen.

Fatigue.—This appears to play a decided part in the causation of compressed-air illness.

Ventilation.—Carbon dioxide within reasonable limits probably has no effect. Poisonous gases such as CO and H_2S, may play a part in the etiology.

The Personal Element.—It is a known fact that many men can decompress rapidly from high pressures, after long exposures, with apparent safety. It is true also that certain men, who appear to be physically fit, have serious symptoms when a slow rate of decompression is employed. In many instances old workmen have had fatal illnesses while subject to apparently the same conditions under which they have worked with safety for long periods. All this leads one to think that there may be some condition or conditions present in certain men which retard or prevent the normal process of desaturation. Furthermore, such conditions may arise in those previously free from them. One can only speculate as to what condition or conditions may be present. It might be some change in the blood, which prevents the free giving off of nitrogen, or some change in the endothelial cells of the capillaries which prevents the elimination of nitrogen. Another possible cause might be sought in some condition in the intestinal tract which prevents the usual elimination of nitrogen through the intestinal wall. A considerable experience leads the writer to believe that the personal element is a large factor in the causation of many serious and fatal cases, and that we must look to its discovery and removal to insure safety in compressed-air work with pressures over thirty pounds +.

Symptoms.—The chief symptom experienced during compression is that of pressure upon the ear drums. Unless the external pressure upon the ear drums can be relieved by causing air to enter the middle ear through the Eustachian tube, by swallowing or by Valsalva's method, this pressure becomes exceedingly painful and may result in rupture of the ear drum unless further compression is stopped. One entering a compressed-air chamber for the first time may experience nervous symptoms, such as increased pulse rate, slight dyspnea, and feelings of apprehension. There may be pallor, due to nervousness. Beyond this, compression has been found to cause no

effects upon either the peripheral circulation, the blood pressure, or the respiration. A sensation of heat and sweating are experienced due to the increased temperature caused by the increasing pressure in the chamber.

Symptoms of compressed-air illness never develop while under pressure. Occasionally symptoms are experienced while decompression is taking place, but by far the greatest number of cases of illness begin after decompression is finished, usually within an hour; although several hours may intervene between the end of decompression and the first onset of symptoms. In some cases onset is delayed as long as ten or twelve hours.

The symptoms are varied. The writer, after a careful study of the reports of 3,692 cases, made the following classification, which also gives the number and percentages of cases falling within each group. The symptoms of the various groups often overlap; but, in this classification, cases were grouped in accordance with their most characteristic symptoms:

A.—Cases showing pain in various parts of the body, "bends"	3,278	or 88.78+ per cent.
Cases with pain also having local manifestations	9	or 0.26+ per cent.
B.—Cases showing pain and prostration.	47	or 1.26 + per cent.
C.—Cases showing symptoms referable to the central nervous system:		
1. Brain (hemiplegia)	4	or 0.11+ per cent.
2. Spinal cord:		
(*a*) Sensory disturbance	36	
(*b*) Motor disturbance	34	
(*c*) Sensory and motor disturbance	10	
	80	or 2.16+ per cent.
D.—Cases showing vertigo, "staggers."	197	or 5.33+ per cent.
E.—Cases showing dyspnea and sense of constriction of the chest, "chokes"	60	or 1.62+ per cent.
F.—Cases showing partial or complete unconsciousness with collapse.	17	or .46+ per cent.
	3,692	99.98+ per cent.

Fatal cases { Group B.—6; Group C.—5; Group F.—9 }

20 or .54+ per cent.

General Symptoms.—Granted that the presence of free gas in the blood or tissue fluids is the cause of compressed-air illness, it is evident that the variety and severity of symptoms manifested will depend upon two factors; namely, the amount of free gas present and the organs or tissues affected. Small gas bubbles in the blood will act as emboli, which may or may not cause symptoms, depending upon what organs or tissues they attack. If the emboli lodge in vital centers of the central nervous system, or in small arteries supplying important organs such as the coronary arteries and small arteries of the brain or cord, or within firm, unyielding tissues, such as ligaments, fasciæ, and periosteum, symptoms will result, and their importance will depend upon the importance of the organ involved and their severity upon the extent of mechanical violence which they exert. In most cases such symptoms will be definitely localized to the organ or tissues involved. If small emboli involve such organs as the liver, spleen, or kidneys, or such tissues as muscle, fat, or loose connective tissue, no symptoms are likely to result. With increasing amounts of free gas in the blood and tissue fluids, the symptoms become more general, and may vary from scattered pain in various parts of the body to rapidly fatal results with coma and collapse. Small amounts of free gas give rise to many of the cases in groups A, C, D and E; larger amounts of free gas to cases in groups B and F.

As to the significance of these symptoms, cases of localized pain, vertigo, and dyspnea seldom if ever are fatal. When the central nervous system is involved, death may result from small emboli in the vital centers of the brain or medulla, or it may follow cord lesions as the result of complications such as cystitis, pyelitis, or pyonephritis, ascending myelitis with diaphragmatic involvement, and pneumonia, bed sores, etc., or permanent paraplegia may result. In most cases patients with pain and prostration survive, although some die. Cases of unconsciousness and collapse are often fatal.

Special Symptoms.—

A. Cases of Pain in Various Parts of the Body.—The characteristic symptom in these cases is pain which is felt in some part or parts of the body. The various locations in which pain may be felt, named in order of frequency, are the legs, the arms, the abdomen, the thorax, the back, and the head. Frequently pain is felt in one or more of these regions, either at the beginning or during the course of the attack. Pain in the extremities is felt most often in or about the joints. The pain may be slight and transient, or it may be severe, lasting in some cases several days. It may be localized or it may radiate, following the course of a nerve; it may be dull or cutting in character, constant or intermittent. Sometimes it is described as deep seated and boring in character as if it were in a bone. The patient may show the usual symptoms of pain such as crying out, facial distortion, pallor, sweating, increase of and sometimes slight irregularity of the pulse, and an indisposition to use the affected part. In some few instances there have been observed local symptoms at the site of pain, such as areas of swelling and subcutaneous emphysema, and brawny edema as of lymphatic obstruction. That these cases of pain are due to local irritation and not to spinal cord involvement, is indicated by: (1) The absence of other signs of cord irritation such as changed reflexes, motor and sensory disturbances, and interference with bladder or rectum control. (2) Local manifestations in some cases. (3) The not infrequent shifting of pain from one part or parts of the body to other parts, which does not happen in undoubted cases of cord lesion.

In accordance with this idea, pain about a joint may be explained by pressure resulting from a small accumulation of free gas beneath a tight fascia or within a bursa or tendon sheath. Neuralgic pains may be due to gas emboli in a nerve sheath. The deep-seated pain can be explained by the presence of gas emboli beneath the periosteum. The chances that gas emboli will involve an extremity or other parts of the body, such as unimportant organs or tissues, are far greater than that they will attack a vital center or a central nervous area. This explains the large proportion of ordinary cases of pain.

B. Cases of Pain and Prostration.—The pain in these cases is usually more or less general, two or three and often all of the extremities being involved. Sometimes there is also abdominal pain. The characteristic symptom in this class of cases is prostration. The patient is often pale and perspires freely, and complains of weakness and sometimes of dizziness. There is often nausea and at times vomiting. The pulse is increased in rate, is small, of low tension, and often irregular. Mottling of the skin is often seen on different parts of the body. In this class of cases the patient is usually conscious, although in the severer ones, semiconsciousness may ensue or even coma. The symptoms are undoubtedly due to considerable quantities of free gas in the circulatory system as shown by the fact that cases of this group sometimes assume the symptoms of group F after a few hours. Moreover, in some of the fatal cases of this type considerable amounts of free gas have been found in the veins at autopsy.

C. Cases Showing Symptoms Referable to the Central Nervous System.—The symptoms in these cases are identical with those due to injuries of the brain

or spinal cord from embolus or hemorrhage. The extent of the lesion, the severity of the symptoms and the ultimate result will depend upon the amount of damage done to the nerve tissues by the gas emboli. Cases may show hemiplegia, with or without aphasia; paralysis or sensory disturbances, singly or combined, of the lower or of all the extremities, with consequent complications such as ascending paralysis, cystitis, pyonephritis, pneumonia, and bed sores. Cases which do not clear up may result in permanent disability or death.

D. Cases Showing Vertigo.—Vertigo is not infrequently a symptom of compressed-air illness. It usually comes on soon after decompression and is often accompanied by other symptoms, such as nausea and vomiting, pains in the extremities or abdomen, dyspnea, and prostration. Cases of vertigo among compressed-air workers have been described by many writers, but Snell first called particular attention to this class of cases, reporting several of them in detail. In most of his cases he found also deafness, which was more or less permanent. He attributed these cases to air embolism in the labyrinth, which in some instances gives rise to labyrinthine hemorrhage. Snell's explanation of the cause of vertigo seems the most reasonable one.

E. Cases Showing Dyspnea and Sense of Constriction of the Chest.—Dyspnea is a not uncommon symptom and while alarming in appearance yields readily to treatment and seldom if ever proves fatal. The subject of one of these attacks appears much like a victim of asthma, and physical examination of the chest often reveals signs resembling those of asthma. Men subject to these attacks of dyspnea often have a moderate degree of emphysema, and after an attack may have signs of bronchitis for several days. These cases are more frequent when blasting is going on in the work. It is difficult to explain these cases, but it seems most reasonable to assign them to local conditions in the lungs, among which one might consider emphysema or bronchitis, irritation by dust or smoke and perhaps by the presence of gas emboli in the lungs themselves. Irritation of the respiratory centers by gas emboli naturally suggests itself as the cause of these cases, but in view of the fact that these cases are so seldom serious, this explanation seems unlikely.

F. Cases Showing Partial or Complete Unconsciousness and Collapse.—These cases are probably a severe form of the cases in group B. as patients who have at first pain and prostration sometimes become unconscious later and die in a condition of collapse. In typical cases of this group attacks occur usually soon after decompression. Unconsciousness and collapse may occur suddenly with few if any premonitory symptoms, or the case may begin with symptoms such as pain in the extremities or abdomen, dizziness, weakness, and convulsions; coma and collapse occurring after a short interval. Mortality is highest in this group of cases.

Some writers have called attention to a class of cases characterized by itching of the skin, either localized to certain parts of the body or general, and have spoken of it as being of frequent occurrence. Few cases of this kind were seen in the work on the Pennsylvania East River tunnels, perhaps because the men in such cases did not apply for treatment.

Mottling of the Skin.—This is seen chiefly in severe cases, usually in those whose symptoms are due to large accumulations of free gas in the blood. It was noted in thirty-eight cases in the study of 3,692 cases. Mottling was present in five of the twenty fatal cases. This mottling varies from an erythematous blotching to a distinctly hemorrhagic eruption. In the hemorrhagic variety the bleeding is probably between the superficial and deep layers of the skin. It varies in extent from small spots to large confluent areas, as large as or even larger than the hand. It may appear on any part of the body, but is seen most often on the abdomen, thorax, and extremities. Erythematous mottling often disappears during or soon after recompression. The hemorrhagic type is more persistent, and fades out gradually in several days in those who recover.

Abdominal Pain.—This is a symptom which is justly feared by workmen in compressed air. It is often experienced with lesions of the cord when it is analogous with the girdle pain of other cord lesions. In many severe cases of collapse and prostration, abdominal pain is experienced either as an initial symptom or during the course of the attack. It is the only symptom in a considerable number of cases, when it usually yields readily to treatment. It seems likely that, while abdominal pain in some cases is due to cord irritation, it is also frequently due to local irritation by gas emboli, either in nerve sheaths or fasciæ of the abdominal wall or in the various abdominal viscera. With simple abdominal pain, one can never feel sure that a serious case is not threatened, for in some cases of paralysis and in a few of the cases of severe prostration and collapse this is the only symptom at first.

Pathology.—Two characteristic conditions are found in most of the fatal cases of compressed-air illness. The first and most characteristic is the presence in the circulatory system of free gas, often in large quantities. The second is the presence of cord or brain lesions, among which the most common are myelitis, meningeal hemorrhage, and hemorrhage into the cord. In addition to the cord lesion, changes due to consequent complication, such as cystitis, pyonephritis, and pneumonia may be found. In a few cases characteristic conditions are not found. In many of these we may assume from their symptoms that small gas emboli have involved vital centers or important organs, without leaving changes which are discoverable.

Von Schrötter makes a summary of 137 fatal cases of compressed-air illness among divers or caisson and tunnel workers, reported between the years 1854 and 1897. The cases are divided into two groups; first those which had exhibited symptoms of central nervous lesion with complications, and resulted fatally after several days, weeks, or months; second, those in which a fatal result followed soon after decompression, which was frequently rapid. Of the first group there were thirty-six cases with twenty autopsies, and in the second group seventy cases with twenty-seven autopsies, of which only eighteen were in detail. In the twenty autopsies falling within the first group there were found lesions of the spinal cord, such as disseminated and transverse myelitis, and hemorrhage in the meninges and in the cord, together with complications, such as cystitis, pyonephritis, bed sores, etc. Of the eighteen autopsies in rapidly fatal cases which were reported in detail, eleven showed the presence, in greater or less degree, of free gas in the circulatory system; in the other seven cases there was hyperemia of the internal organs, in all there was hyperemia of the lungs, in some a condition resembling that of suffocation, and in one Bright's disease.

In the twenty fatal cases reported from the Pennsylvania East River tunnel work, five fell within the first group, and of these two came to autopsy and showed lesions of the cord and complications; fourteen fell within the second group and of these, in twelve autopsies reported, eight showed the presence of free gas in greater or less degree in the circulatory system.

Treatment.—Of the various means of treatment which have been employed, but one has proved of undoubted benefit. This is recompression, which was first proposed by Pol and Wattelle, who demonstrated its effects on animals. Its first practical employment was made by E. W. Moir on the old

Hudson River Tunnel. It is now generally employed when men work in compressed air, being required by law in several countries. Recompression is carried out in a medical air-lock consisting of an air-tight steel cylinder about six feet in diameter and twelve feet in length, closed at one end. At the other end is an entrance by means of an air-tight door, which opens inward. The cylinder is divided into two compartments by means of a transverse partition, which has a door opening toward the inner compartment. Compressed-air pipes and outlet valves supply both chambers, so that the pressure can be raised or lowered from either chamber. This arrangement enables a physician or attendant to enter or leave the chamber in which the patient is being treated without disturbing the pressure of that chamber. Valves are also placed outside the lock so that the pressure can be regulated from without. The inner chamber is fitted with two bunks, one on either side, upon which patients can lie, and with electric lights, telephone, clock, pressure gage, thermometer, and electric heater. A means of ventilating the inner chamber should also be supplied. Heavy glass windows are placed on a line in both doors, so that one can watch from outside the patient, the pressure gage, and the thermometer.

Recompression should be instituted as soon as possible after the appearance of symptoms, the pressure being raised quickly to a point equal to the working pressure. Relief of symptoms when afforded, usually occurs before this point is reached. Soon after reaching full working pressure, decompression should be begun at a rate not less than one pound per minute and in severe cases, much more slowly. During decompression, the patient, if able to do so, should move about and exercise the affected part. In severe cases massage and passive motion should be administered by an attendant, and in unconscious cases, artificial respiration should also be performed. Various stimulants help in severe cases. If symptoms return after one recompression, a second recompression should be made. It is sometimes necessary to recompress several times before permanent relief is obtained. In cases of simple pain, where there is a return of symptoms after recompression, relief, frequently permanent, may be obtained by the use of counterirritation with liniments, the vibrator, or the Faradic current, or by hot applications.

The sooner, after the appearance of symptoms, recompression is begun, the more likely is it to afford relief and the relief to be permanent. The failure of the treatment to afford relief is to be explained by the fact that recompression has not been employed before the air emboli have done permanent injury to the tissues.

The results of treatment in 3,692 cases at the Pennsylvania East River tunnels were as follows: In 3,278 cases of pain in various parts of the body, about ninety per cent. got relief from one or more recompressions.

In forty-seven cases of pain and prostration, thirty-eight were relieved or cured by recompression, all ultimately recovering; six showed only temporary improvement and died. The other three refused the medical lock, and recovered after illnesses of about a week.

In eighty cases with symptoms referable to the central nervous system, the results were as follows: 4 cases of hemiplegia all cleared up permanently with recompression; of 36 cases of sensory disturbance, 34 were relieved by recompression, 2 refused the medical lock and were improved by medical treatment; of 34 cases of motor disturbance, partial or complete paralysis of the legs, 23 were benefited by recompression and either cleared up at once or recovered later; in 11 recompression caused no improvement and of these, 5 ultimately died, 3 had permanent spastic paraplegia, and 3 were lost sight of; of 10 cases of sensory and motor disturbance, 9 were permanently relieved, the other was improved, but the final result was not learned.

In 197 cases, having vertigo, with or without vomiting, pain, prostration, and dyspnea, 108 had complete relief from recompression, 82 had partial relief from recompression, and 7 refused the medical lock; none of these men died.

In 60 cases of dyspnea all cleared up with one recompression except 2 which required a second recompression.

In 17 cases of partial or complete unconsciousness and collapse, 8 were cured or relieved by one or more recompressions, 9 had little or no relief and died. Oxygen given to several of these severe cases during recompression, afforded no appreciable benefit.

Prophylaxis.—How to prevent compressed-air illness is a most important question. Recompression, while an efficient means of treatment in mild cases, often fails to prevent disability and death in severe ones. If high pressures are to be used, all means should be employed to prevent illness. These should consist of thorough medical examinations of workmen and especially of new candidates. In cases where "green" men must work in high pressures, twenty-five pounds + or over, preliminary tests should be given and, if satisfactorily passed, a short working shift should first be tried. Careful supervision of the workmen should be exercised, and occasional reexaminations made, especially after any absence from work. The men should be instructed as to the dangers of rapid decompression, should be made to move about during and after decompression, and should be warned that neglect to seek medical advice at once upon the appearance of any symptoms may result disastrously. They should also be informed of the bad effects of excesses of all kinds, of improper hygiene, and of intercurrent illness.

The following table indicates briefly what can be done by medical examinations and supervision to eliminate the predisposing causes:

Predisposing Causes	*Can be Prevented*
Age (improper)	Yes.
Build (fat).	Yes.
Organic disease.	To a large extent.
Alcoholism.	To a large extent.
Newness to work.	Partly.
Fatigue.	No.
Ventilation (bad).	To a large extent.
Personal element.	No, not with our present knowledge.

The chief means of preventing illness must be found in the arrangement of shifts and decompression periods to suit the pressures. In some countries, these are regulated by law. This is true in New York State. As time goes on, further legislation will be necessary. In studying the causes of compressed-air illness one should not forget that many factors play a part and that, since the human organism is concerned, it is not a purely physical question. The results of comparatively few experiments with animals should not be looked upon as final. In the same way, the results under certain conditions with comparatively few men should not be considered conclusive. While much may be done by proper regulations to diminish cases of illness and death in compressed-air work, the writer believes that, when pressures of two or more atmospheres are being used, it should be classed as a dangerous occupation on account of individual conditions not now understood, which he has called the personal element. Frederick L. Keays.

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Cajuput, Oil of.—*Oleum Cajuputi.* A volatile oil distilled from the leaves of *Cajuputa leucodendron* (L.) Rusby (fam. *Myrtaceæ*). This species is a rather small fragrant tree, with irregularly growing slender branches and a thick, soft, exfoliating bark. The leaves are bright, smooth, narrow, entire, pointed at each end, parallel nerved, and often oblique or curved; they are twisted upon their petioles so as to stand with their edges vertical, like phyllodia. The tree is a native of numerous islands in the Indian archipelago, especially of Borneo, Celebes, and Amboyna. It is also extensively found, if a broad view is taken of the species, in Australia and on the mainland of Asia. Most of the oil is obtained from Celebes and exported by way of Javan or Indian ports.

Oil of cajuput is extracted on the spot from the fresh leaves, which are first softened by maceration in water and then subjected to distillation in rude copper stills. It is filled into once-used wine and beer or other European bottles for exportation. It was first introduced into Europe in the early part of the eighteenth century.

It is a pale green, transparent, mobile fluid, with a fragrant mint or camphor-like odor, and bitterish aromatic taste. It has the usual physical properties of the essential oils. It is very similar to its near relative, oil of eucalyptus, containing the same constituent, cinecol of which the U. S. P. requires the presence of not less than fifty-five per cent., a process of assay being prescribed. Terpineol and other bodies are also present. Specific gravity of the oil, 0.915 to 0.925 at 77° F. It is soluble in alcohol in all proportions, and in one part of eighty per cent. alcohol, the solution being neutral. The green tint is generally ascribed to some compound of copper received from the still, or introduced into the oil intentionally. The color may be separated by several methods of rectification, the oil obtained being clear and white.

Action and Use.—Cajuput has the stimulating properties of camphor and the essential oils in general, and stands between the most irritant of them, like oil of turpentine, and the milder mint oils. It is more extensively used in the Indies and Eastern islands than here—in some places being given for nearly everything, but is particularly popular for colics, diarrheas, and even cholera, as well as for chronic rheumatism, chronic vesical catarrh, etc. Here it is not often given internally, but has no doubt some value in non-inflammatory intestinal disturbances, where an aromatic stimulant and antispasmodic is needed, being in these cases very much like camphor, and like this may be very suitably combined with opium. Externally it is a mild rubefacient, and a good ingredient for stimulating liniments in chronic rheumatism, sprains, etc.; it may be also useful for psoriasis, scale eczema, etc.; and is a fairly efficient parasiticide. As a stimulant diuretic in chronic vesical catarrh it is as good as most others of its class. Cajuput is the basis of numerous toothache apd earache drops. It is often adulterated. Dose from ℥ij. to viij. (0.12–0.5) dissolved in spirit, suspended in mucilage or syrup, or dropped on a lump of sugar. There are twenty or thirty drops to the gram. H. H. Rusby.

Calabar Bean.—See *Physostigma.*

Calabar Swellings.—Transient, smooth, ovoidal tumors which occur on various parts of the body in both native and European inhabitants of Africa within the endemic area of *Filaria loa*, and which are almost certainly caused in some way by that parasite.

Thompstone says that the swellings, as seen in tropical West Africa, "are about the size of half a goose egg, painless, though somewhat hot, both objectively and subjectively, not pitting on pressure, and usually disappearing in about three days. They come suddenly and disappear gradually, and occur in any part of the body." They never suppurate. Manson, who proposes the theory that they are caused by the female *Filaria loa* emptying her uterus of larvæ into the connective tissue, has aspirated serum from a Calabar swelling in each of two cases; in one case without result, and in the other finding larvæ of *Filaria loa.* He suggests the possibility that the larvæ found in the second case might have been in the small quantity of blood unavoidably taken in the passage of the needle. The blood of the patient contained larvæ of both *Filaria loa* and *Filaria perstans.*

The mechanism of the production of Calabar swellings is an unsolved problem. They are seen in some patients who are not proved to harbor *Filaria loa.* A large proportion of the patients are known to be infected with this parasite. The adult *Filaria loa* lives and moves about in the connective tissue, often producing irritation. These facts, considered with the coincident geographical endemicity of calabar swellings and *Filaria loa* make the causal relation of the latter to the former almost certain.

J. F. Leys.

Calamus.—Sweet Flag. The dried rhizome of *Acorus calamus* L. (fam. *Araceæ*). A monocotyledonous perennial with a thick, fleshy, long and branched horizontal rootstock, and a few very long (0.5 to 1 m.) and narrow linear equitant leaves. The flowering scape is also long and flattened, resembling the leaves, and bears at its apex a straight, solid, fleshy, cylindrical spadix from five to ten centimeters

Fig. 1183.—Rhizome of *Acorus calamus*, showing cicatrices of adventitious roots. (Baillon.)

long. Flowers perfect, small, crowded. A long, leaf-like bract or "spathe" arises at the junction of the spadix and scape, and, proceeding in a straight line, looks like a continuation of the scape, while the really terminal spadix is diverted to an angle with the axis, and appears to be lateral. Sweet flag grows in swamps throughout almost the whole north temperate zone.

All parts of the plant are slightly aromatic, the leaves least so, but for medicinal use the rhizome only

is employed. It should be gathered in the autumn or spring, washed, cleaned, and dried. The drug of most of the foreign Pharmacopœias is peeled or scraped before drying; but while the appearance is improved by this process, the strength and quality are deteriorated, since most of the activity resides in the bark, and this is not authorized by our Pharmacopœia. Although it grows in great abundance in the swamps of the United States, a large portion of what we use is imported from Europe.

Calamus comes in pieces of from ten to thirty centimeters or more in length, by one or two centimeters in thickness (from 4 to 12 in. × ½ in.); it is shriveled and lightly flattened, marked by frequent and very distinct rings and remains of leaf scales, and below is covered with the circular scars of the roots. It is pale or reddish brown externally, white and

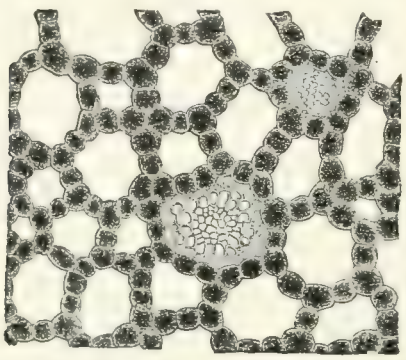

Fig. 1184.—Transverse Section of the Rhizome of *Acorus calamus*. (Baillon.)

spongy within. Its texture is very light, being traversed by large air spaces separated by only a single row of cells. A cross-section shows these as large holes, and the walls as a lace-like reticulation, varied with occasional woody bundles (see Fig. 1071). The oil cells are like those of the general parenchyma, but larger and are generally situated in the angles formed by the confluence of three or four of the partitions, as shown in the section.

The principal constituent is the *oil*, of which it contains two or three per cent., a yellowish or brownish very fragrant liquid of specific gravity 0.9. It also contains the glusoside *acorin*, which is a soft, resinous substance, with a bitter, aromatic taste, resin, starch, tannin, gum, and a minute amount of the alkaloid *calamine*.

Calamus is a pleasant tonic, aromatic-bitter, applicable to all the purposes for which such remedies are used. Dose, ℥ss.–i (2.0–4.0); of the oil, from gtt. x. to gtt. xv.

Henry H. Rusby.

Calcification.—Calcium phosphate and calcium carbonate in some combination as yet unknown are found in invisible soluble forms in practically all of the tissues and fluids of the normal body. In the bones and in the so-called "brain sand" (*acervulus cerebri*) alone, do they occur in a solid form, either combined with magnesium phosphate in an intimate relationship to the organic matrix of the bones or as laminated chalky spheroids having a cellular matrix in the pineal gland and choroid plexus. Under pathological conditions of the most varied kinds salts of lime are deposited in a solid and visible form in tissues other than bone or are precipitated from the secretions or excretions, appearing as minute or coarse granules, platelets or larger masses. Such a pathological *calcification* may occur in single cells or cell-groups (ganglion cells, renal epithelium, heart-muscle), in the ground substance of the connective tissues (cartilage, fibrous connective tissue), in elastic fibers, in foreign bodies (parasites, inclusions), and in the organic material of certain secretions (concretions, calculi). Deposits of lime-salts in the tissues are usually considered under the head of calcification, while concretions and calculi are separately treated. The connective tissues, by far, are most frequently the seat of calcification, while gland cells (liver, pancreas), striped and unstriped muscle, and nervous tissue are much less frequently affected. Pathological new formation of bone also is not rare, but there is a great difference between ossification and calcification in that in the latter there is not an organized matrix with a definite arrangement of bone corpuscles and blood-vessels, lacunæ and canaliculi. Nevertheless, there is a close relationship between the two processes, inasmuch as true bone formation is not rare in calcified leiomyomata, calcified areas in blood-vessels and lymph-nodes, and in calcified fibrous connective-tissue stroma. There is a difference of opinion as to the chemical identity of the lime-salt composition of calcification and that of ossification. Some writers (Von Kossa, Kockel, Adami) hold that in bone there is a definite ratio between the calcium and magnesium salts and the phosphoric and carbonic acids, while this is not true of calcifications. Others (Wells) consider that there is a close similarity of composition in bone and calcification as far as the ime-salts are concerned; and the present tendency is to accept the view that chemically the lime-salts of pathological calcification have the same composition as those of bone. The fact that the areas of calcification often contain an abundance of iron (Berlin-blue or ammonium sulphide reactions) has been regarded by some writers as an essential point of difference between ossification and calcification; but a similar iron-content is found in many fetal bones, as well as in some pathological ossifications, while in some calcifications it is absent. Apparently the iron is present in the early stages of ossification or calcification, or may even precede these processes. The nature and significance of the iron combination with lime-salts are unknown. The iron may act as a mordant for the lime deposit.

Summing up the differences between calcification and ossification, the main points are these: ossification occurs only in connective tissues, calcification in all cells and tissues. In calcification the cells are dying, or of a low vitality, as in the extracellular interstitial substances, or dead, and the deposit of lime-salts is, in fact, an inert foreign body instead of a specialized tissue, as in bone formation. In calcification the lime-salts never become evenly diffused through the organic ground substance, as in bone, but remain in granules, clumps, or masses.

Etiology.—Pathological calcification depends upon changes in the character of the cells or tissue-elements, whereby they acquire an increased affinity (*calciphilia*) for the lime-salts circulating in the blood. As far as we know calcification never occurs in any normal tissue but bone. A pathological calciphilia characterizes, however, all dead, and many degenerating or dying tissues and extracellular, interstitial substances of poor vitality. As far as human pathology is concerned *calcification indicates always severe metabolic changes of the tissue and the death of the cells.* Only in experimental work with animals (guinea-pigs) can a visible heaping-up of granules of lime-salts be produced in living cells (epithelium of renal tubules and gastric glands after temporary ligature of the vessels and inhibition of the excretion of lime-salts). Such a condition is only temporary and may be followed by a complete restoration of the cells to the normal. Moreover, it is more closely related to the formation of concretions than to tissue calcification. According to Wells, the calcification of renal epithelium and tube casts,

which is experimentally produced by temporary anemia and by certain poisons, is probably analogous to the calcification of organic material in urine. Upon just what chemical or physical conditions the abnormal calciphilia of dead and dying tissues depends is not yet clear. That the calcium salts must come from the blood or lymph is certain; calcification is not a precipitation of lime-salts normally held in solution in the affected area. Nor is it a precipitation from the blood due to changes in composition of the latter. That an increase in the calcium content of the blood is not essential is also certain, but the calciphilia is the more easily satisfied the greater the calcium content of the blood. Hence in conditions like osteomalacia, and extensive resorption of bone in syphilis and malignant neoplasms of bones, as well as in the osteoporosis of old age, the removal of lime-salts from the bones and the increased lime-content of the blood favors the deposit of lime-salts in the kidneys, lungs, gastric mucosa, cartilages, and blood-vessels (*calcareous metastasis* of Virchow). Even in these conditions the increased calcium-content of the blood alone is not sufficient to cause calcification, the tissues concerned always present pathological changes (hyaline change, atrophy, etc.) that determine the seat of the calcification. Whether these local changes are chemical or physical in character is not yet determined. At any rate we can safely conclude from all existing evidence that a metastasis of lime-salts into normal cells and tissues does not occur, and that there is no essential difference between calcareous metastasis and other forms of calcification.

Granting, then, the existence of a calciphilia due to an injured (necrobiotic or necrotic) state of the cell, and that these retrograde changes are essential to pathological calcification, the withdrawal of lime-salts from the circulating blood by such areas of tissue degeneration may be explained in a number of ways:

1. The calcification may be due to physical conditions favoring absorption of salts, the least soluble salts accumulating in excess, without direct chemical interaction with the matrix, the conditions in the latter being such that the salts are thrown into insoluble forms.

2. The formation of calcium-binding substances within the degenerated area.

3. Increased alkalinity in the degenerating tissues causing a precipitation of the salts in the fluids passing through them.

4. Precipitation of the calcium from the fluids passing through the tissues as a result of the complete utilization of the proteids in the fluids.

The first three theories attract the most attention at the present time, particularly the second one. Various substances having a high affinity for calcium, such as phosphoric acid, fatty acids, carbonic acid, deutero-albumose and other proteins have been suggested as the calcium-binding substances that may be present in degenerating or necrotic areas. The formation of calcium albuminates is urged by a number of writers as the chemical affinity playing the chief rôle in calcification, the protein acting as a weak acid, and later replaced by carbonic or phosphoric acid. It is also worthy of note that the three organs most frequently showing the so-called calcareous metastasis constantly secrete acids, the lungs carbonic acid, the stomach hydrochloric, and the kidneys uric acid. Some forms of calcification, at least, are associated with the formation of calcium soaps (fat necrosis, concretions in adipose tissue). As the result of fat-splitting (fatty degeneration or fat necrosis) the free fatty acids combine with calcium to form calcium soaps (combinations of fatty acid, calcium, and protein). Later the fatty acids are replaced by carbonic or phosphoric acid. To what extent this method of formation occurs in the other forms of calcification is not yet certain. Klotz and others hold that the first step in the formation of pathological calcification is the production of calcium soaps that afterward become changed into phosphates and carbonates. In support of his view he showed experimentally that collodion sacs containing fat or fatty acid inserted into the peritoneal cavity of a rabbit would in a few days contain amounts of calcium far in excess of that found in the body-fluids of the animal. Calcium percolating into the sacs becomes fixed. Wells opposes this view and holds that there is no essential difference between the processes of ossification and pathological calcification. The close relationship between fatty degeneration and calcification may be taken as an argument in favor of Klotz's views, but the problem must still be regarded as unsettled. At the present time we do not even know the nature of the calcium combinations in the blood, and until we know more concerning the combinations of calcium and protein, or the disintegration compounds of the latter, and their occurrence in calcified areas, we cannot hope to understand the nature of calcification.

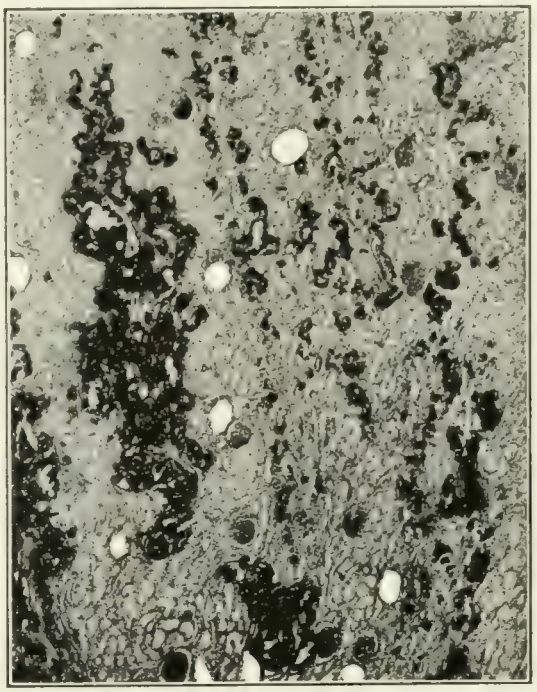

Fig. 1185.—Calcification of Kidney in a Case of Leukemia Treated for a Long Period with Röntgen-ray Irradiation. Low power.

The evidence in favor of a physical deposition of the lime-salts is also unsatisfactory. It is true that sterilized cartilage exhibits a specific absorption affinity for lime-salts similar to that shown by gelatin disks toward other crystalline substances in solution, but the fact is not sufficient to explain all the phenomena of calcification and ossification.

Occurrence.—Calcification occurs as a result of the most varied pathological processes. Anything that may cause necrobiosis or necrosis of cells may cause a deposit of lime-salts secondary to the primary injury. Necrosis, fatty degeneration, and hyaline degeneration most frequently precede calcification. Areas of necrosis, infarcts, old abscesses, tubercles, gummata, necrotic tumors, old pus, fibrinous exudates, retained placenta, dead fetus (lithopedium),

old blood clots, and thrombi (arterioliths and phleboliths) may undergo calcification. Poisons that cause degeneration (fatty or cloudy swelling) or necrosis of renal epithelium give rise to calcification (mercuric chloride, aloin, bismuth, carbolic acid, phosphorus, acetate of lead, copper sulphate, copper acetate, cyanide of mercury, potassium chlorate, iodine, iodoform, chloroform, formalin, chromates, etc.). Poisoning with oxalic acid may give rise to deposits of calcium oxalate in the kidney. Scar tissue or newly formed connective tissue (adhesions, thickenings) in chronic inflammations (pericardium, pleura, meninges, etc.) that has undergone a hyaline change is particularly likely to undergo calcification.

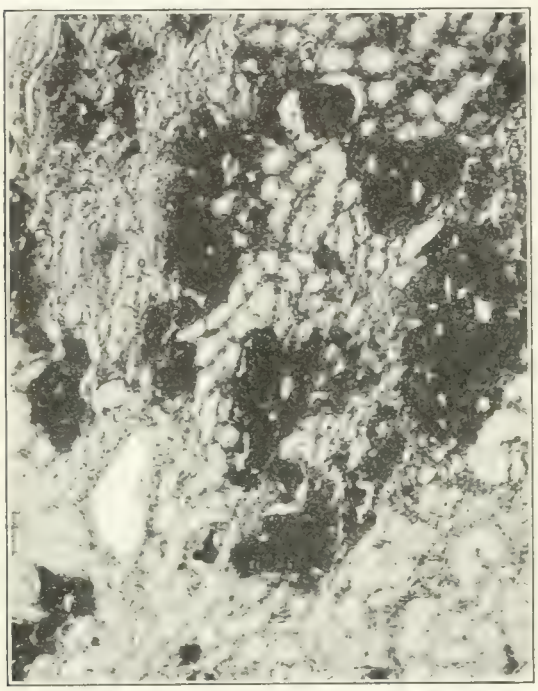

Fig. 1185.—Calcification of the Kidney Following Prolonged Röntgen-ray Irradiation. High power.

Large calcareous plaques may be found in the pleura or pericardium. Likewise connective-tissue hyalin in sclerotic blood-vessels, sclerotic heart-valves, interstitial tissue of the thyroid, healed tubercles, foreign-body cysts, neoplasms, gummata, etc., very frequently becomes calcified. Deposits of lime-salts are always present in the mature placenta (infarcts, thrombi, etc.) and must be regarded as physiological (senile). The retained placenta or dead fetus may become partly or wholly calcified. In old age deposits of lime-salts occur in the sclerotic blood-vessels, ground substance of the cartilages (costal, laryngeal), lungs, capillaries, kidneys, and gastric mucosa ("calcareous metastasis" associated with osteoporosis). In cases of osteomalacia and bone absorption due to malignant neoplasm or syphilis, a similar deposit of lime-salts occurs in tissues of low vitality. In the kidneys lime-salts may be deposited in hyaline glomeruli, blood-vessels, connective tissue, and in the epithelial hyalin contained in cysts or tubercles. The deposit of lime-salts in the kidney may be so great that the tubules of the medullary pyramids appear as white radiating stripes (chalk infarct). An extreme calcification of the kidney occurs in cases of leukemia treated by Röntgen irradiation, the lime-salts being deposited in the necrotic epithelial cells of the tubules. (See Figs. A and B.) Lime-salts are often deposited in the corpora amylacea of the prostate and lungs, and in the colloid of the thyroid. Deposits of lime-salts occur more rarely in the elastic fibers of the lungs, heart muscle fibers (following fatty degeneration), central portion of the liver lobules (after chloroform poisoning, eclampsia, etc.), seminal vesicles, testis, medulla of adrenal, and brain. In the last named the ganglion cells near a hemorrhage, infarct, abscess, or traumatic injury often become calcified. In pathological conditions of the meninges (chronic meningitis) as well as in old age, the brain-sand concretions (corpora arenacea) are often greatly increased in number and occur also throughout the spinal meninges. Deposits of lime-salts in the pancreas and spleen are very rare.

Calcification is very common in neoplasms, partly as a sequel to degenerative changes (necrotic and degenerating myofibroma and lipoma, necrotic areas in carcinomas and sarcomas, epithelial pearls in squamous-celled carcinoma, etc.), and partly as a feature of the tissue forming the tumor (hyaline formations in psammoma and cylindroma, cartilage and cartilage-like interstitial substances in chondromas, myxochondromas, osteomas, and the malignant tumors derived from them). Concentric, striated calcareous spherules and spicules are characteristic formations in the psammoma of the dura mater. They are formed by the deposit of lime-salts in hyaline cell-masses and connective-tissue bundles, and resemble the normal "brain-sand." The cysts of parasites within the tissues (echinococcus, trichina, etc.) become calcified after the death of the parasite.

Gross Appearance.—Calcified areas may appear to the naked eye as white, chalky foci, either hard or crumbling, dull or glistening, diffuse or sharply circumscribed. In the latter case they appear as concretions imbedded in the tissues or free in tissue-spaces, or body-cavities. The affected area shows an increased consistence, and in cutting it, a grating sound or sensation is produced. Glistening spicules are sometimes seen on the cut surface (heart, kidney), and a lung with extensive calcification of its capillaries has the consistence and rough "feel" of a sponge. Calcified myofibromata may be harder than bone and give a high ringing note when struck. Arterioliths and phleboliths may be as hard as marbles and also give a clear ringing sound when dropped onto a solid surface.

Microscopical Appearances and Microchemical Reactions.—In unstained sections the lime-salts appear as opaque or translucent, highly refractive, fine or coarse granules, or larger, obscurely crystalline or angular lumps or masses, that are often confluent in plaques, or form globular, polyhedral, or mulberry-like concretions within the tissues. By reflected light calcified areas usually appear white and glistening, as if crystalline. Very small concentric calcareous bodies (calcospherites) are found often in nervous tissue, tumors, cysts, colloid of the thyroid, prostatic concretions, etc. They also occur in normal tissues. They are apparently identical with the larger "brain-sand" concretions. Deposits of lime-salts are insoluble in ether and dilute caustic potash. They are slowly soluble in formalin. When treated with acids (hydrochloric) they dissolve, the carbonate with the formation of gas bubbles. When dissolved in sulphuric acid characteristic crystals of calcium sulphate are formed. The treatment of sections containing lime-salts for five minutes with a solution of pyrogallic acid (2 : 80) to which one part of caustic soda has been added, then thorough washing in distilled water, causes a decolorization of normal tissues, while the calcified areas appear dark brown. Von Kossa's reaction is also used for the demonstration of calcium phosphate (phosphoric acid). The sections are

treated for five minutes in a five-per-cent. solution of silver nitrate, which forms a yellow phosphate of silver that upon standing is reduced and metallic silver is precipitated, giving a black color to the smallest particles of the calcium phosphate. The simplest and best staining reaction for lime-salts in ordinary work is simple staining with hematoxylin (hemalum, Delafield's, etc.) and counterstaining with eosin. The calcified areas (carbonate and phosphate, not oxalates) appear deep blue-violet or blue-black. Differentiation with acid alcohol should not be carried out when staining for calcification, as the lime-salts are easily dissolved out. Picric acid is an especially good fixative for all tissues containing lime-salts, as even large deposits may be easily cut without tearing after such fixation, and the specific reaction with hematoxylin still can be obtained in the affected areas. In large and old masses of calcification the lime-salts often stain with hematoxylin only about the borders of the calcified areas, the central portions remaining clear and translucent.

Significance of Calcification.—Pathological calcification is always a retrograde process, a deposit of lime-salts following some degeneration (cloudy swelling, fatty degeneration, epithelial and connective-tissue hyalin) or necrosis, due to some acute or chronic injury to the cells and tissues.

Reaction to Calcification.—In the neighborhood of calcified areas there is often a definite proliferative reaction, with formation of foreign-body giant-cells, encapsulation, etc. Deposits of lime-salts also sometimes apparently cause a bone-forming stimulus upon the neighboring connective tissue, and true ossification occurs. Very frequently, however, areas of calcification show no signs of reaction in the neighboring tissues.

Lessened Calcification, Decalcification, or Halisteresis.—New-formed bone may not undergo normal calcification (rachitis, osteoid tissue in neoplasms, etc.), or the lime-salts may be withdrawn from developed bones (osteomalacia, bone-syphilis, neoplasms of bone, etc.). The nature of these pathological disturbances of calcification is not understood, nor do we know the nature of the physiological osteoporosis of the bones in senility. The various theories proposed up to the present time fail to explain all of the facts.

Aldred Scott Warthin.

Calcium.—Calcium is a bivalent metal belonging to the group of the Alkaline Earths. It is found only in combination, chiefly as limestone, chalk, marble, alabaster, etc. Its symbol is Ca, and its atomic weight 40.

General Medicinal Properties of Compounds of Calcium.—In the group of metallic elements represented by the metals of the alkalies and of the earths, calcium is distinguished, in its relations with the animal economy, by its comparative inertness. Of late years it has been found that two of the salts of calcium (the chloride and lactate) have some influence on the coagulability of the blood; also that the chloride has a resolving effect on glandular swellings and a tonic action on the heart and blood-vessels (see *Chlorides*). The medicinal characteristics of lime preparations as a class are lowness of diffusion power, and hence difficulty of absorption, slight local tendency to repress secretion, and slight constitutional tendency to oppose degenerative processes in tissues. Individually, the calcium compounds differ greatly in their properties, and thus arise many individual therapeutic applications, to be noted under the several preparations.

The Compounds of Calcium Used in Medicine.—The compounds of calcium that enter into the pharmacopœial preparations containing the metal are the *oxide, hydroxide, carbonate, phosphate, sulphate, hypophosphite, chloride, bromide, sulphide* (in the preparation *sulphurated lime*), and the compounds, whatever they be, that form the substance called *chlorinated lime*. In the present article will be discussed only the *oxide, hydroxide, carbonate, phosphate,* and *sulphate*. For the other compounds above cited, see, respectively, *Hypophosphites, Chlorides, Bromides, Sulphides,* and *Chlorine*.

Calcium Oxide.—Calcium oxide, CaO, in the form of the ordinary "lime," or "quicklime" of commerce, is official under the simple title *Calx*, Lime. It is officially described as "hard, white or grayish-white masses, which, in contact with air, gradually attract moisture and carbon dioxide, and fall to a white powder; odorless, of a sharp, caustic taste. Soluble in about 760 parts of water at 25° C. (77° F.), and in about 1600 parts of boiling water; insoluble in alcohol. It forms readily soluble salts with diluted acetic, hydrochloric, or nitric acids. When sprinkled with about half its weight of water, calcium oxide becomes heated, and is gradually converted into a white powder (calcium hydroxide or slaked lime). When this is mixed with about three or four parts of water, it forms a smooth magma (milk of lime). Its aqueous solution has an alkaline reaction upon red litmus paper" (U. S. P.). Because of the strong affinity of lime for water, it should be kept in tightly closed vessels in a dry place. Lime is obtained from some of the varieties of native calcium carbonates, or from white marble or oyster shells, by calcining.

Physiologically the importance of quicklime lies in the fact that because of its intense affinity for water it is caustic. To a moist surface it is powerfully escharotic, and since the product of the caustic action (slaked lime) is a nearly insoluble solid, the action is non-spreading.

In practice, quicklime is rarely used by the surgeon, except in the form of the composite preparation, *potassa with lime* (Vienna caustic), for whose description see under *Potassium*.

Calcium Hydroxide.—Calcium hydroxide, $Ca(OH)_2$, is the familiar substance, *slaked lime*, which forms in the shape of a white powder as the product of the chemical reaction between lime and water. The reaction is attended by the development of a high degree of heat. Slaked lime is not official in the United States Pharmacopœia under any distinctive title, but the preparations into whose composition it enters are defined as preparations of lime simply. Slaked lime is a soft, white, bulky powder, of a mawkish, alkaline taste, and having the solubilities detailed above in the pharmacopœial description of lime. Although a powerful free base, it is not caustic to living tissue, because of its difficult solubility in water. Combining as it does, therefore, the qualities of harmlessness and high alkalinity, it is valuable as an antidote—so far as antidotes go—in poisoning by acids. Especially is it to be selected in cases of poisoning by oxalic or sulphuric acid, because of the great insolubility of the salts it makes with these several acids. For medicinal purposes, proper, slaked lime is used in the valuable pharmacopœial preparation commonly known as *lime water*, but officially entitled *Liquor Calcis*, Solution of Calcium Hydroxide. This is simply a saturated aqueous solution of slaked lime, easily made by any one by stirring freshly slaked lime into water—fairly pure water free from salts—in any proportion greater than 1 to 750. The vessel containing the resulting solution is to be kept tightly stoppered, with the excess of undissolved lime retained. After the settling of the undissolved portion, the clear, supernatant liquor may be drawn off in small quantities, for use, by decanting or siphoning. The object of having an excess of lime lies in the fact that lime water has a great affinity for carbon dioxide, absorbing this gas from the atmosphere and forming with it the insoluble

calcium carbonate. By such reaction the lime of lime water gradually becomes exhausted, but by the device of keeping in the containing vessel an excess of lime, the water of the solution recharges itself therefrom as fast as it loses strength by carbonating, and the solution of lime is thus maintained steadily at saturation. Lime water is "a saturated, aqueous solution of calcium hydroxide. . . . . The percentage of calcium hydroxide varies with the temperature at which the saturated solution is prepared, being about 0.17 per cent. at 15° C. (59° F.), the percentage diminishing as the temperature rises" (U. S. P.). Although clear when first made, lime water, upon keeping, is certain to become turbid from absorption of carbon dioxide from the atmosphere, and the formation thereby of calcium carbonate. If, however, there be, as above advised, an excess of lime in the bottle, the turbidity does not mean loss of strength, and a sample so affected is perfectly good for medicinal purposes. Lime water is incompatible with alkaline carbonates, sulphates, borates, salts of ammonia and the metals, acids and acidulous salts, and astringent vegetable decoctions or infusions.

Lime water is, of course, alkaline, and at the same time is, physiologically, locally bland and soothing to irritation, with a tendency to check secretion. Taken internally it operates to allay gastric irritability and to control diarrhea, especially when the diarrhea is caused by acidity of the intestinal contents. From the conjunction of properties named, lime water is an excellent alkaline wash in skin disease, and is a standard remedy to subdue vomiting and combat the diarrhea of acidity. In its internal use by far the best way of giving is in mixture with fresh, ice-cold milk. In such mixture, even when "half and half" in strength, the disagreeable lime taste is almost wholly lost, while at the same time the medicinal efficacy of the lime is enhanced, and the patient is nourished by the milk. In obstinate vomiting, indeed, nothing surpasses the administration of small quantities of ice-cold lime water and milk, frequently repeated, to the exclusion of all other medicine and nutriment. In ordinary cases, the lime water need not be in greater proportion to the milk than one part to two, three, or four. If the stomach be not too sensitive, such mixtures may be administered quite freely; but yet the *habitual* use of lime water in milk by milk-fed individuals, such as infants, is objectionable. For occasional use, lime water is so innocent that it is hardly possible to assign any exact dose, but a tablespoonful generally suffices for a single giving, to be taken in at least an equal measure of water or milk. A special application of lime water is based on the fact that the tissue of false membranes immersed in the solution rapidly disintegrates. Hence the practice with some to spray the throat, in croup or diphtheria, with atomized lime water. In such procedure, however, it must be remembered that in the amount of spraying practically possible, the quantity of lime water brought into contact with the membrane is very small, and the duration of the contact short.

Lime water, although decidedly alkaline, is not readily absorbed, and consequently is useless for constitutional alkalizing. For such purpose, alkalies of high diffusion power, such as the basic compounds of potassium or lithium, must be used rather than lime.

Besides lime water, the United States Pharmacopœia offers, as a preparation of lime in solution, *Syrupus Calcis*, Syrup of Lime, Syrup of Calcium Hydroxide. This syrup is made by treating a triturated mixture of lime and sugar with boiling water, and bringing the solution after filtration to the standard strength of 6.5 per cent., by weight, of lime. In this procedure the lime and sugar chemically unite, and the product, while retaining the alkalinity and physiological properties of free lime, is yet much more soluble in water, as the percentage strength of the syrup attests. Syrup of lime is therefore, medicinally, a sweetened and at the same time a strong solution of lime, and may be used for the internal applications of lime water, only in much smaller dose—one-eighth, namely, of what would be given of the latter-named preparation.

For local application of the soothing properties of lime solutions, an excellent and ingenious preparation of lime is official in the United States Pharmacopœia under the title *Linimentum Calcis*, Lime Liniment, often called *Carron oil*, from the Carron Iron Works, in Scotland, where the liniment acquired great reputation for the treatment of burns among the workmen. The preparation is simply a mixture, in equal parts, of lime water and linseed oil, whereby a lime soap is formed, which being insoluble makes an emulsion with the considerable excess of the oil prescribed by the formula. The oil, however, readily separates from the aqueous portion, and hence the preparation should be well shaken each time before use. Lime liniment combines the protection of a fixed oil with the alkaline and soothing properties of lime, and makes an excellent dressing for painful affections of the skin, such as burns, both allaying pain and promoting healing. It is applied clear.

Calcium Carbonate.—Calcium carbonate, $CaCO_3$, is represented in the United States Pharmacopœia by two preparations. *Creta Præparata*, Prepared Chalk, is the native article freed from most of its impurities by elutriation; and *Calcii Carbonas Præcipitatus*, Precipitated Calcium Carbonate, is the carbonate obtained as precipitated from a solution of calcium chloride by reaction with sodium carbonate. Prepared chalk is in the form of powder, or of little conical pellets, and the precipitated carbonate is always in the condition of a very fine soft powder. Both preparations are permanent in air, odorless and tasteless, and insoluble in water or alcohol, although soluble, with effervescence, in hydrochloric, nitric, or acetic acid.

Calcium carbonate closely resembles slaked lime in its properties, but, being a salt, is less strongly alkaline, and, being wholly insoluble in neutral fluids of aqueous basis, is, locally, absolutely bland. It is medicinally applicable, in a general way, for the same purposes as lime water, and, in addition, because it is a bland, soft, and alkaline absorbent powder, it makes an excellent "dusting powder" to apply as a dressing to skin affections in which the cutaneous surface is moist and tender. Internally the carbonate is available as an antidote to acid poisoning, especially if the acid be sulphuric or oxalic, and is of use to correct idiopathic acidity of the *primæ viæ*, and to allay nausea and check diarrhea. Being perfectly innocent, either of the forms of the salt may be given freely. For ordinary use in digestive derangements the single dose ranges from gr. x. to xlv. (0.65–3.0). The medicine may be given as a powder, but administration in mixture is more common. The following pharmaceutical preparations are official in the United States Pharmacopœia: *Pulvis Cretæ Compositus*, Compound Chalk Powder. This consists of three parts of prepared chalk, two of powdered acacia, and five of powdered sugar, mixed. This powder is probably official as the basis for making the next named preparation, but yet is itself a convenient chalk powder for direct prescription. *Mistura Cretæ*, Chalk Mixture. This is compounded of two parts of the foregoing compound chalk powder and four parts each of water and cinnamon water. The sugar and acacia of the compound chalk powder dissolve and the slightly viscid solution resulting is capable, when shaken, of holding the chalk in suspension. The preparation should be freshly made for use, and should be shaken each time before dispensing a dose. It makes a very conven-

ient basis for diarrhea mixtures, especially in cases of diarrhea with acidity. It may be given in tablespoonful doses.

Calcium Phosphate.—This salt, $Ca_3(PO_4)_2$, is the phosphate commonly called *bone phosphate*. It is official under the title *Calcii Phosphas Præcipitatus*, Precipitated Calcium Phosphate, and is made by dissolving the phosphate of bone ash by means of hydrochloric acid, and then precipitating it from the solution by the addition of water of ammonia. Such precipitate, washed and dried, presents itself as "a bulky, white, amorphous powder; odorless and tasteless; permanent in the air. Almost insoluble in cold water; partly decomposed by boiling water, which dissolves out the acid salt; almost insoluble in acetic acid, except when freshly precipitated; easily soluble in hydrochloric or nitric acid; insoluble in alcohol" (U. S. P.). When freshly precipitated and still moist this phosphate also dissolves wholly in lactic acid.

Calcium phosphate is an important normal ingredient of the animal body, being the calcareous element of the bones and teeth. The use of the salt in medicine has been its internal administration in conditions of disease when there appears to be a deficiency of the substance in the proper tissues, either from assumed lack of supply or from want of power of assimilation. Such conditions are illustrated by rickets, mollities ossium, caries of the teeth, and possibly by scrofula and phthisis. But, as often happens in medication based on purely chemical considerations, the clinical results frequently fall short of the expectation, so much so that many practitioners put but little faith in the present remedy. Very likely the lack of effect of calcium phosphate is principally due to the difficulty of determining the absorption of the salt, partly because of the salt's entire insolubility in other than acid menstrua, and partly because of its low diffusion power. But inasmuch as the phosphate is wholly innocent, locally and constitutionally, it may with propriety be tried in cases in which it seems indicated theoretically. A dose of gr. x. to xxx. (0.6–2.0) may be given three times a day, larger doses probably being useless through lack of absorption. A convenient form of the medicine is the official preparation of the United States Pharmacopœia, entitled *Syrupus Calcii Lactophosphatis*, Syrup of Calcium Lactophosphate. Precipitated calcium carbonate is dissolved in dilute lactic acid, and to this solution phosphoric acid is added. After certain necessary trituration, the solution of the lactophosphate is filtered, sweetened, and flavored with orange-flower water, and then brought to standard strength by the addition of water. Twenty-five parts, by weight, of calcium carbonate are used to make one thousand measures of the syrup. Should a gelatinous precipitate tend to form upon keeping, a fluidram of hydrochloric acid may be added to each pint of the syrup, The preparation may be given in doses of from two to four teaspoonfuls, representing from gr. iij. to vi. (0.2–0.4) of phosphate.

Calcium Sulphate.—This salt, $CaSO_4,2H_2O$, is used in medical art only in the making of plaster-of-Paris dressings. Calcium sulphate occurs native in several conditions, the commonest being the salt combined with two molecules of water constituting the substance *gypsum*. The valuable property of gypsum is that when dehydrated and treated with water it recombines with the latter, and in such combining sets in a hard, dry mass. Gypsum is dehydrated by heat, which should not exceed 120° C.; for if carried too high (above 204° C.) the gypsum—called then technically *dead-burnt*—recombines with water but slowly and the product does not solidify. As properly dehydrated and pulverized the product is a white powder, without odor or taste, called *burnt gypsum* or *plaster-of-Paris*. Plaster-of-Paris is official in the United States Pharmacopœia under the title *Calcii Sulphas Exsiccatus*, Exsiccated Calcium Sulphate. Mixed with two parts of water, plaster-of-Paris makes a soft, creamy paste, which in the course of from fifteen to twenty minutes gradually stiffens, until at last it sets into a perfectly hard and dry mass. During the setting a moderate degree of heat is evolved (not beyond the range perfectly bearable by the human skin), and the mass very slightly expands. Applied, therefore, as a casing to a limb, the dressing may be perfectly fitted without fear of shrinkage upon setting. After setting, the plaster-of-Paris neither softens nor dissolves by treatment with water, the solubility of calcium sulphate in water being only about 1 part in 500. For use in surgery the plaster-of-Paris paste may be applied by smearing it upon the bandaged limb so as to form a casing, but a far better way is to impregnate a flannel bandage thoroughly with the dry plaster, roll it loosely, and when the dressing is to be fitted dip the roller into a vessel of water until bubbles cease to be evolved and then apply in the usual manner, but without reverses. Before so applying, however, the skin should be protected by a plain bandage, or, where appropriate, by a thread glove or a stocking.

Plaster-of-Paris should be kept in well-closed vessels, else, attracting moisture from the atmosphere, it will become partially hydrated.

EDWARD CURTIS.
R. J. E. SCOTT.

Calculi.—See *Concretions*.

Calculi, Cutaneous.—See *Milium*.

Caledonia Springs. — POST-OFFICE. — Caledonia Springs, Ontario, Canada. Hotel, the Grand Hotel.

ACCESS.—From Montreal and Ottawa by Canadian Pacific Railway.

Analysis, by Sterry Hunt. In one thousand parts:

Solids.	Gas Spring.	Saline Spring.	White Sulphur Spring	Duncan or Intermittent Spring.
Chloride of sodium	6.9675	6.4409	3.5430	12.2500
Chloride of potassium	0.0309	0.0296	0.0230	0.0305
Chloride of calcium	...	...	...	0.2870
Chloride of magnesium	...	...	...	1.0338
Bromide of sodium	0.2150	0.0169	0.0100	...
Bromide of magnesium	...	...	...	0.0238
Iodide of sodium	0.0005	0.0014	...	...
Iodide of magnesium	...	...	...	0.0021
Sulphate of soda	0.0053	0.0048	0.0183	...
Carbonate of soda	0.0485	0.1762	0.4558	...
Carbonate of lime	0.1480	0.1175	0.2100	0.1264
Carbonate of magnesium	0.5262	0.5172	0.2940	0.8672
Carbonate of iron	Trace.	Trace.	Trace.	Trace.
Alumina	0.0044	...	0.0026	...
Silica	0.0310	0.0425	0.0840	0.0225
	7.9773	7.3470	4.6407	14.6433

These springs are carbonated saline, mildly charged with carbonic acid gas. There escapes with the water of the Gas Spring a large amount of carbureted hydrogen gas. The water of the White Sulphur Spring contains sulphureted hydrogen equal to about one cubic inch per gallon. The springs are situated on a level plateau which extends for many miles in all directions, the country being open and well cultivated. These springs have been purchased by the Canadian Pacific Railway. The company has rebuilt the Caledonia Springs Hotel and conducts it with the same care and excellence as the other hotels of this well-known system. All modern methods for utilizing the waters are at hand, and a physician and expert attendants reside at the hotel. The hotel is open throughout the year.

The Caledonia Springs are the best known of Canadian mineral springs and are resorted to by large numbers from Canada and the United States, particularly from the South. In addition to the water consumed at the springs, an up-to-date bottling establishment has been erected and large quantities are bottled and sent to all parts of Canada and the United States. BEAUMONT SMALL.

Calendula.—MARIGOLD. The dried ligulate florets of *Calendula officinalis* L. (fam. *Compositæ*). These florets are strap-shaped, nearly half an inch long, three-toothed, hairy upon the tube, of a bright yellow color, pistillate, with a two-branched style. The odor is characteristic, the taste aromatic and bitterish. They contain a little volatile oil and an amaroid, with resin and an abundance of the bright yellow coloring matter, *Calendulin*, which is inactive. The drug possesses very slight aromatic-bitter properties, but is chiefly used for coloring purposes. It is now much less used than formerly, and will doubtless be omitted from the next edition of the Pharmacopœia. The dose is gr. xv. to xxx. (1.0–2.0).

The herb possesses similar properties, but is even weaker and contains much more mucilage. It has been used similarly, as well as for making poultices. Through an error, this, instead of the florets, was incorporated in the preceding edition of the Pharmacopœia. HENRY. H. RUSBY.

California Geysers.—Sonoma County, California. Hotel and cottages. This marvellous region is located in the northeastern part of Sonoma County, about 100 miles north of San Francisco, 16 miles from Cloverdale, and 26 miles from Calistoga. Formerly tourists rode on horseback for many miles to visit this realm of fumaroles and solfataras, which is situated about 1,700 feet above the sea level; but, thanks to the push and enterprise of our Western civilization, it may now be reached in a comfortable auto stage via Healdsburg over excellent mountain roads. It is a good plan to go by way of Cloverdale and come back by way of Calistoga, as all the grandeur and beauty of the surrounding country may thus be seen. The following entertaining account of a visit to the geysers is taken from Dr. Anderson's work:

"Leaving Cloverdale after luncheon, comfortably seated in our stage, with an experienced and accommodatingly communicative driver, who takes pleasure in pointing out the many objects of interest, we soon cross the Russian River and commence the ascent. The hills and mountains are robed in evergreen verdure of indigenous flora, gigantic oaks, and towering pines. Here and there the huge boulders and rocky cliffs stand out in bold relief, and as we wind up and around the mountain sides, with the Pluton River many hundred feet below, basking and smiling in the afternoon sun, and rippling along its moss-covered banks and bright-pebbled bottom, with here and there a minature cascade and waterfall, we feel that words cannot describe the grandeur of the scenery. . . . .

"As we gain in altitude the view becomes more and more extended, until our eyes leap with vivid interest from peak to peak and valley to valley for miles around, feasting upon the beauties of nature. Some two or three miles down the cañon, before we reach the geysers, our attention is called to the large white or yellowish-white banks across the cañon. They are known as sulphur banks, and consist of deposits of sulphur and cinnabar, with incrustations of salts of sodium, potassium, magnesium, sulphur, etc. . . . . Near these sulphur banks are found the famous Indian Springs, at which Edwin Forrest camped for one season and was completely restored to health."

The waters are diuretic, laxative, and antacid, and are valuable in dyspepsia, torpidity of the liver and bowels, and in renal and cystic diseases. (See table for analysis.)

Near by are the real "Indian Mud Springs," which are highly extolled in the treatment of chronic rheumatism, gout, arthritis, and synovitis, and scrofulous and cutaneous contaminations. (See table.)

". . . . . After a few more horseshoe curves have been passed and several more magnificent landscapes have been mentally photographed on the brain, we reach the geyser resort. The many cosey cottages, the hotels and grounds, are situated in a leafy dell on the side of the mountain opposite the Geyser Cañon. The huge oaks and pines afford pleasant shade to the commodious verandas as we sit and enjoy the pure,

ANALYSIS OF WATERS FROM SEVERAL SPRINGS AT THE CALIFORNIA GEYSERS.

Contents per United States gallon, expressed in grains.	Lemonade Spring. Temp. 103° F.	Witches' Caldron. Temp. 212° F.	Acid Spring. Temp. 140° F.	Alum Spring. Temp. 130° F.	Iron Geyser Creek, below Alum Spring. Temp. 96° F.	Spring on side of hill near river. Temp. 138° F.	Iron Spring north of hotel. Temp. 70° F.	Indian Spring (second). Temp. 101° F.	Mud Indian Spring. Temp. 100° F.	Spring little above Indian Spring. Temp. 105° F.	Hot sulphur water above bathhouse. Temp. 104° F.	Devil's Tea-Kettle. Temp. 212° F.
Potassium bisulphate	7.53	0.42	1.14					0.21				
Potassium sulphate									17.12			98.16
Sodium bisulphate	53.91	39.82	9.62	5.14								
Sodium sulphate					3.15	3.23		3.29			2.36	
Sodium carbonate								1.40				
Calcium sulphate		6.98	4.44	3.81	5.34	1.10	3.32		6.42	8.72	.65	4.36
Calcium carbonate								7.35				
Calcium silicate						10.18						
Calcium borate											6.62	
Magnesium sulphate	40.73	9.62	91.29	34.49	16.66		2.52		59.33	41.12		39.09
Magnesium carbonate								15.47				
Magnesium silicate						15.46						
Magnesium borate											17.31	
Iron sulphate	12.25		16.63	7.34	.08	.11				28.81	.16	
Iron carbonate							.12	.07				
Aluminum sulphate	32.02	2.04	20.62	63.82		.20			22.78	118.78	2.39	31.16
Alumina		.27			.89		.17	.18				
Free sulphuric acid	31.82		154.37	6.45					32.30	5.75		110.64
Hydrochloric acid	1.19											
Silicic acid	16.50	4.37	21.11	17.26	3.50	17.25	.99	5.42	12.25	18.08	8.63	12.83
Sulphureted hydrogen	Sat.	Sat.	Sat.	Sat.	Sat.			Sat.	Sat.	Sat.	Sat.	Sat.
Boric acid			Str.	Trace.							Str.	Traces
Total	195.95	63.52	319.22	138.31	29.62	47.53	7.12	33.39	150.20	221.26	38.12	296.24

dry, invigorating, and exhilarating mountain air and picturesque scenery which surround us on every side."

The geysers are wonderful and picturesque exhibitions of the nearly extinct volcanic forces slumbering beneath the romantic "Devil's Cañon." The region covers an area of about 400 acres, most of the activity, however, being confined to the "Devil's" or "Geyser" cañon, comprising about sixty acres. Collectively, the springs, hot and cold, flow about 100,000 gallons daily. There are about one hundred different mineral springs. Natural steam "Hammam" mineral baths are features of the resort. There is also a swimming pool of mineral water.

From the above analyses made by Prof. Thomas Price it will be observed that at the geysers can be found probably as great a variety of mineral waters as at any other place on the continent, or perhaps in the world.

Near Litton's Station, in Sonoma County, some few miles from Geyserville, is a pleasant resort known as the "Geyser Spa" or "Soda Springs." The surrounding country is picturesque, and the climate mild and salubrious. A large number of people go to Geyser Spa every year. The waters are highly esteemed for their antacid, diuretic, and aperient properties. The following analysis was made by Dr. Winslow Anderson in 1888:

One United States Gallon Contains:

Solids.	Grains.
Sodium chloride....	8.93
Sodium carbonate.	4.97
Sodium bicarbonate.....	21.16
Sodium sulphate.....	2.60
Potassium carbonate....	Trace.
Magnesium bicarbonate.....	9.03
Magnesium sulphate	1.14
Calcium carbonate...	4.90
Ferrous carbonate..	2.09
Silica.....	3.75
Organic matter....	Trace.
Total solids....	58.57

Carbonic acid gas, saturated.

A previous analysis made by Bauer and Price yielded results almost identical with Anderson's.

Emma E. Walker.

California Poppy.—See *Eschscholtzia*.

California, Southern.—In this article only a brief and general account of the climate of Southern California will be given, as the principal resorts and sections will receive especial mention under their respective heads, in regular alphabetical order.

Southern California is an irregular area of territory, equal in extent to England and Wales, lying between latitude 35° 40′ and 32° 30′, with a coast line of 330 miles. It is bounded on the north by the Tehachapi Mountains, which are spurs of the coast ranges and Sierra Nevada; on the east by the Colorado River; on the south by the Mexican frontier; and on the west and southwest by the Pacific Ocean. In the western portion is the southern coast range, forming the eastern boundary of the *coast plain*, which contains numerous beautiful valleys, such as the Santa Clara and Santa Buena Ventura. This coast plain extends for 150 miles, and is from 15 to 25 miles in depth. Between the coast range and the Sierra Madre and San Bernardino ranges lies the *interior plain*, 200 miles in length and from 15 to 30 miles in depth. Here is the great San Gabriel Valley, which has been called the Lombardy of America, and numerous lesser valleys. "Between the coast plain and the long interior valley, the coast range of mountains is broken, and, opposite the Los Angeles plains, entirely disappears for a space. The whole country becomes thus a great open coast-land facing the south, and with the high Sierra for a background." ("California of the South," by Walter Lindley and J. P. Widney, 1888.) North and east of the Sierra, or inland range, lie the Mojave and Colorado deserts. It is with the resorts on or near the coast, or with those in the interior plain, that we have especially to deal as climatic stations, such as Santa Barbara, San Diego, Coronado Beach, on the coast; or, farther inland, Riverside, Redlands, San Bernardino, and others. The soil is composed largely of disintegrated granite, which is sandy and porous, and in many localities there are also large patches of adobe or red clay. The main features of the climate of Southern California are warmth, equability, a large amount of sunshine, and a small amount of annual rainfall. "Taken as a whole," says Professor Hilgard, "Southern California corresponds in its climatic features and adaptation to the Mediterranean region of Europe and Africa; a grand Riviera with a partial background of the desert as well, where the date palm and ostrich find a congenial home, and alluvial plains equalling in riches the famed delta of the Nile."

"Warm winters, comfortably cool summers, very low rainfall, and rainfall so distributed as to divide the year into a dry and a so-called rainy season, almost unparalleled preponderance of cloudless weather, and (in consequence of the low latitude) a long duration of the daily sunshine in winter—all these are characteristic of every portion of Southern California. In comparative humidity of the atmosphere lies the chief difference between its coast stations and those lying at a greater or less distance from its coast line" (Huntington Richards).

"The warmth and equability of this climate depends," says Dr. C. F. Williams ("Aero-Therapeutics," 1894), "upon three factors: its southern latitude, its protection by the various mountain ranges from cold northerly or easterly winds, and the influence of the Pacific, and especially the warm ocean currents which wash the shores of the Western States."

There exists a certain misapprehension regarding the matter of dryness of this climate. For example, as good an authority as Lindsay refers to it as "intensely dry." Williams calls it a "dry, warm climate," and Remondino remarks that "every term in the meteorological vocabulary relative to moisture and dryness has been conscientiously applied to the region." The fact is that the coast districts, like all other coast resorts, exhibit the features of a marine climate, one of which is a large amount of moisture, and upon this fact, as we know, depend the coolness and equability characteristic of such a climate.

If one would find real dryness he must, as Solly says, seek it beyond the mountains in the desert country. If, however, "he seeks more days of sunshine and opportunities for outdoor life, with a more equable temperature and an average humidity a little greater than that of New York or Boston, he can find what he desires at Santa Barbara or San Diego." Even as far inland as Riverside, more than fifty miles from the coast, the humidity is appreciably greater than at Aiken, for example, and very considerably greater than at most of the Colorado, New Mexico, and Arizona resorts. Still further, one must bear in mind the fact, as Solly says, "that, in spite of the great amount of sunshine during the day in California, the foggy and damp nights and mornings take up a great part of the twenty-four hours." This authority notes the following observation made by himself at Redlands: "On one occasion when at 4:30 P.M. the relative humidity, as indicated by the hygrometer, was fifty-five per cent., at 6 P.M. it had increased to eighty per cent." "The difference between noonday and midnight temperature," says Kate Sanborn ("A Truthful Woman in Southern California," 1895), "between sun and shade, is something to be learned and guarded against."

Climatic data.	San Diego, latitude, 32° 43′; longitude, 117° 10′.						Santa Barbara, latitude, 34° 28′; longitude, 119° 41′.						Los Angeles, latitude, 34° 3′; longitude, 118° 5′.					
	Jan.	April.	July.	Nov.	Winter.	Year.	Jan.	April.	July.	Nov.	Winter.	Year.	Jan.	April.	July.	Nov.	Winter.	Year.
Temperature—																		
Average or normal..	53.6°	57.7°	67 1°	58 2°	54 5°	60.4°	51.2°	60 5°	66 8°	56.0°	54 01°	60 7°	54 1°	58 0°	71.1°	62 0°	53 5°	62.0°
Average daily range.	17.3	14 1	11 6	18 1	16	14 3	18	18	19	25		19 1	20.1	20 2	23.1	24.5		
Mean of warmest	61 8	65 3	73 5	66 8	.	.	57 8	65	69 2	62 3			62 9	69 2	82	70.7		
Mean of coldest.....	44 5	51.2	61 9	48.7			42 8	52	69.7	53			42.8	49	58 9	46.2		
Highest or maximum	78	87	86	85			83	86	89	82			82	94	98.1	86		
Lowest or minimum.	32	39	54	33			38	11	41	40			30	39	51 2	34 2		
Humidity —																		
Mean relative.....	71.2%	72 4%	76.4%	66.4%	70.9%	72 9%	71%	67%	72%	64%		73%	62 9%	70.1%	69.4%	57.3%	63 6%	66 6%
Precipitation—																		
Average in inches...	1 85	0 68	0 02	0 70	6 04	9 49	3.7	1.4		1 6	11 77	17 6	3.9	1 3		.95	8 65	18
Wind—																		
Prevailing direction	N.E.	W.	W.	N.W.	N.E.	W.						W.	N.E.	W.	W.	N.E.	N.E	W
Average hourly velocity in miles.....	5.1	6 6	6.3	5 1	5.4	5.9	4.3	5.3	5 1	3		4 6	5 5	5 4	4 9	4.9	5.4	5.1
Weather—																		
Average number of clear days.....	11 3	10 2	8.2	13 5	33 5	122.7	24	16	27	13		231	17.5	10 2	10 4	18.8	.	171.3
Average number of fair days	11.2	11.9	16 1	10	33.7	155 1	1	6	3	9		63	8.5	12 5	19 7	9.3	26.6	144.8
Average number of clear and fair days.	22 5	22.1	24 3	23 5	67.2	277 8	25	22	30	22		294	26	22.7	31.1	28.1	74 5	316.1

Riverside, 60 Miles from the Coast, 850 Feet Above Sea Level.

	Jan.	April.	July.	Nov.	Year.
Mean monthly temp..	53.1°	61.2°	77.0°	62.2°	62.0°
Maximum temp.....	78.2	89.2	101.2	89.2	
Minimum temp.....	32.7	39.2	60.5	39.5	
Relative humidity....	67%[1]	56%[2]	63%[3]	76%[4]	67%
Precipitation—					
Average in inches....	3.27	1.43	.	1.35	10
Wind					
Prevailing direction..	.	.	S. W.	.	W.
Weather—					
Average number of clear days....	16	20	29	15	(1890) 208
Average number of fair days	.	.	.	.	105
Average number of cloudy days....	14	9	1	10	52

From July, 1885, to July, 1886, there were 280 absolutely clear days, and 38 days of rain or showers.

[1] For the spring of 1888. [2] Summer of 1888. [3] Autumn of 1888. [4] Winter of 1888.

The accompanying tables of climatic data of San Diego, Santa Barbara, Los Angeles, and Riverside exhibit, so far as such statistics can, some of the principal climatic features of this region. As there is no government weather station either at Santa Barbara or at Riverside, the figures for these places must be considered as only approximately correct. A general similarity will be noted in the climates of all these places. As one goes inland the relative humidity is seen to lessen. The number of fair and clear days is very large, the precipitation very small, the prevailing winds are from the west, and there is no great wind velocity. At Riverside, a distance of fifty miles or more from the coast, the maximum temperature, especially in summer, is seen to increase. A peculiarity of this climate, not indicated in climatic charts, is the great difference between the character of the atmosphere during the day and during the night. At night the humidity is greatly increased, an example of which has already been noted in the case of Redlands. This increase of moisture by night renders the air chilly and raw, and in many cases would prevent the free admission of night air into the sleeping-rooms. Even during the day this chilliness is experienced in passing from the sunshine into the shade, and when the wind blows.

Another peculiarity is the frequent night fog, present not only on the coast, but extending many miles up the valleys. These fogs, which are most prevalent during the spring and summer, appear about nightfall and disappear during the early forenoon. Occasionally they persist during a part or the whole of the day. The annual mean average number of foggy nights at Los Angeles, for thirteen years, was 57. In 1891 there were 22 fogs in San Diego, 12 in 1893, and 26 in 1894. At Santa Barbara there were 73 fogs in 1894.

The rainfall, which is small in any event, except on the highest summits, occurs in the winter, which is the rainy season. This rainy season, however, varies very greatly from year to year. Sometimes the rain is delayed for weeks, and then it may rain continuously for days. One cannot predict from the annual average precipitation what the rainfall will be for any single year. For instance, Los Angeles has a normal precipitation of 18 inches, but in 1881 it was 5.6 inches, and in 1884, 40.5 inches. The normal of San Diego is 10 inches, but it has had a minimum of 3.71 inches and a maximum of 25.97 inches. The heaviest rainfall occurs in the months of December, January, and February. Even January, however, may be a very dry month. In the desert regions there is almost no rain. Thus, for instance, at Indio the annual average for nine years was 2.32 inches. It is to be remembered, as Solly points out, that even in the rainy season the monthly rainfall is not usually more than the normal monthly rainfall for Eastern cities, and there are longer periods of fine weather. "The welcome rains," he continues, "bring a vivid green to the brown valleys and hills, and the beautiful 'procession of flowers,' which continues from December to May, enraptures Eastern visitors."

Regarding the winds there is one point which the tables do not show, and which, as Widney says, most impresses the observer in his study of this meteorological factor, and that is, their regularity. One can be assured that at certain seasons of the year the wind will blow from a certain quarter, and rise at a certain time each day. Further, he knows that if the wind blows from a certain quarter, certain climatic conditions will follow: if it blows from one direction a moist atmosphere and rain will result; if from another, a dry atmosphere, cold in winter, hot in summer; if

from still another, there results clear, cool weather with moderate moisture.

Much has been written about the great variety of climate to be found in Southern California. For instance, one author writes thus: "Within a few hours from any given point one may obtain the climate to his liking." Such sweeping statements are manifestly misleading, for where in any inhabitable locality in Southern California can be found the cool, dry air furnished in the elevated plains of Arizona, New Mexico, or Colorada, at such resorts as Tucson, Santa Fé, and Colorado Springs?

In addition to the favorable climatic conditions of this marvellous section of country, there is the fascinating charm of beautiful and diversified scenery —sea coast and mountain—with varied and luxuriant vegetation.

A great variety of fruits of both tropical and temperate regions are produced here: oranges, lemons, grapes, figs, olives, guavas, pineapples, pears, peaches, and strawberries all the year round. Riverside has its famous Magnolia Avenue and orange groves; Sierra Madre its vineyards; Santa Monica its ostrich farm; and San Diego its beautiful Coronado Beach, which Charles Dudley Warner calls, in "Our Italy," "An unique corner of the earth." The temperature of the sea water is 60° F. or more throughout the year, so that one can enjoy sea bathing at any time of year. There are also abundant opportunities for hunting, fishing, camping, riding, and almost every kind of outdoor diversion. If we consider all this, and the fact of an almost continuous sunshine, we can understand how outdoor life becomes a delight hardly imaginable until realized.

Here, also, one can not only take the open-air treatment, but, while doing so, can, if strength and other conditions permit, occupy himself in making a new home, and in light and pleasing work in garden and vineyard. As Dr. Richards says: "Southern California is not only a good winter residence, but a health-giving and health-restoring home for residence all the year round."

Formerly—and to a large extent at the present time —Southern California was considered one of the most favorable resorts in this country for pulmonary tuberculosis, and probably more invalids suffering from this disease frequented this region than any other class. Moreover, no discrimination appears to have been made regarding the stage or condition of the pulmonary trouble suitable for this climate. In the writer's opinion, this will not be so much the case in the future, since experience is proving more and more conclusively every day that the sanatorium treatment of consumption is affording the best results, and that the situation of the sanatorium, climatically considered, does not make so much difference, provided pure air, a dry soil, freedom from high winds, and a reasonable amount of sunshine are assured. Almost every State can offer these simple climatic conditions, and hence can have its own sanatorium.

This plan, moreover, possesses the further advantage, so much emphasized by the German phthisiotherapeutists, that the consumptive is treated under a climate like that in which, if cured, he will continue to live. So far as statistics are at hand, however, sanatorium treatment in this climate has shown excellent results, quite equal to those of institutions in other favorable climates. It is the combination of the favorable climate and the well-conducted sanatorium that produces results.

In the writer's opinion, Southern California, in the future, will be visited not so exclusively by consumptives as heretofore, but by the large class of invalids requiring a mild, equable, sunny climate, with ample opportunity for outdoor life and diversion; such as the feeble from age or inherited weakness, convalescents from various acute diseases, those suffering from malaria, catarrhal affections, chronic bronchitis, renal and cardiac diseases, scrofulous children, and those individuals who are in the quiescent state of pulmonary tuberculosis without pyrexia. Finally, to this list must be added that increasingly large number of persons who desire to escape the inclemency of a Northern winter.

The conditions for which this climate is unfavorable or doubtful are tuberculosis with acute symptoms, certain diseases of the nervous system, laryngeal tuberculosis, eczema, asthma, and rheumatism.

There has been much exaggerated and immoderate writing on the climate of Southern California, not infrequently from selfish and commercial reasons, as also from superficial and inadequate knowledge. One physician writes of San Diego that it presents "all the factors requisite in a perfect climate." Another, writing of Pasadena, says that it is "the greatest all-the-year-round-health resort in the world," and so on.

Such wild statements, generally made without any accompanying meteorological data, seem quite unnecessary in regard to a climate which in fact and truth possesses so many points of excellence as does that of Southern California. EDWARD O. OTIS.

Calisaya.—See *Cinchona.*

Calliphora.—The genus to which the blue-bottle fly or blow-fly belongs. *C. vomitoria* is the common species in this country. See *Insects, poisonous.*

A. S. P.

Callosity.—*Synonyms*: Callositas, Tyloma; Tylosis; Callus; Keratoma; (*Fr.*) Durillon.

DEFINITION.—A circumscribed thickening and welding of the horny layer produced by intermittent friction or pressure.

Callosities are congenital or acquired. The congenital callosities, however, are now usually discussed separately under the heading of Keratodermia or Tylosis Palmæ et Plantæ. The latter are diffuse or circumscribed keratomata, usually symmetrically distributed over the palms or soles, or over both, springing from an apparently normal skin or surrounded by a red areola. Arsenic from prolonged use often causes a similar condition.

Peculiar symmetrical horny hypertrophies are sometimes associated with certain neuroses or unknown constitutional conditions; these are often preceded by mild inflammatory symptoms. The so-called syphilitic keratodermias should probably be placed with the latter class. The term callosity is more properly applied to the acquired form, which is essentially a result of external irritation by friction, by *intermittent* pressure, or rarely by chemicals. *Continuous* pressure or friction causes active inflammatory reaction, either vesiculation, or pustulation, or sloughing. The result of this milder trauma is best seen upon the hands of mechanics, oarsmen, wood-choppers, and those whose occupations necessitate this irritation, as yellowish or yellowish-brown, circumscribed, round, or irregularly shaped flat or raised patches of thickened skin that are hard and resistant to the touch. They occur usually over the bony prominences or bursæ, and spring from apparently normal skin.

Callosities may occur upon any portion of the body subjected to the exciting factor. On the soles, while there are a number of factors involved such as ill-fitting shoes, etc., I have called attention elsewhere to the frequency with which callus is associated with malpositions of the feet, that is, weak foot, flat-foot, etc. It is well known that callus and warty growths are not uncommon concomitants of hyperidrosis, at least the hyperidrosis is the first symptom of the relaxed condition of the foot.

This thickening of the horny cells is an effort of nature to protect the more delicate underlying structures. Histologically there is probably no actual increase in the production of epithelial cells but a "welding" together (Unna) of the pre-existing horny cells, by the friction, into a homogeneous horny mass; thus the cells normally thrown off are retained, producing an apparent increase and an actual thickening. Except in those cases in which the condition results from a more violent trauma, no marked inflammatory symptoms, aside from a slight dilatation of the vessels, are seen.

The acquired callosites can be differentiated from the keratodermias by the history and symmetry of the latter, though it must be remembered that in those who are particularly susceptible, very little friction may produce a marked callus.

The syphilitic conditions of the palms and soles usually begin in the center and not over the bony prominences, spread peripherally, and at some points the horny layer is often split up or undermined.

The treatment of callosities is first to remove the cause, whatever that may be. When callus occurs on the soles it would be proper to examine the foot as to the existence of any malposition, and if such should be the case its correction should be undertaken at once. To soften and remove the thickened horny layer salicylic acid is the remedy *par excellence*. It can be used in form of a plaster (ten to twenty per cent.) or in flexible collodion (℥ss.–℥i.). Either should be applied for several days, when the affected part is immersed in very hot water for several minutes and the dead, macerated cells removed by gently scraping with a curette or dull knife blade. This procedure is repeated as often as necessary until the skin is reduced to its normal thickness, when a mild tar application will effectually complete the cure.

WILLIAM A. HARDAWAY.

Calorimetry.—See *Heat, Animal.*

Calumba.—COLUMBO. "The dried root of *Jateorhiza palmata* (Lam.) Miers (fam. *Menispermaceæ*)." (U. S. P.)

The columbo plant is a large, perennial climber, often ascending to the tops of the loftiest trees, with a rounded, thick, yellow rhizome, from which numerous fleshy roots are given off. These roots are fusiform, resembling long dahlia or sweet-potato roots. They are dug up, sliced transversely, and dried in the shade.

Columbo is a native of Mozambique, Zanzibar, and the adjacent lands of tropical Africa, and is said to be cultivated.

The dried sliced root has a very characteristic appearance. It is in circular discs from one to five or six centimeters in diameter (½ to 2 in.), and from one-fifth to one-half inch in thickness; the edge (surface of the root) is brown and rough; the flat surface (sections of the root) lemon-yellow, and depressed in the middle from collapse of the soft, thin-walled cells of the pith in drying. A dark circle marks the cambium, and one or two indistinct circles of woody bundles can be seen within it. The tissue is chiefly parenchyma, loaded with starch.

Columbo contains several bitter principles. Its one per cent. of alkaloid, long regarded as berberine, is now known to consist of at least three alkaloids, *calumbamine*, *palmatine*, and *jateorhizine*. There is, in addition, from a half to one per cent. of the amaroid *calumbin*. *Calumbic acid* is also bitter. Columbo also contains a little volatile oil, a large amount of starch, pectin, and gum, five per cent. of resin, and a little fat and wax. It is free from tannin, so that it possesses the merit of mixing with iron, in tonic mixtures.

None of the active principles of columbo are in any degree poisonous. They unite in making it a simple bitter tonic.

The dose of the powdered root is gr. viii. to xv. (0.5–1.0), but it is seldom so employed. A fluid extract and a twenty-per-cent. tincture are official, the dose of the former being fl. ℥ss–fl. ℥i(2.0–4.0), of the latter fl. ℥ ss–fl. ℥ ij (2.0–8.0).

HENRY. H. RUSBY.

Calx.—Lime, the official title of calcium monoxide, CaO. It occurs in hard white masses and on the addition of water is converted into calcium hydroxide, slaked lime, $Ca(OH)_2$. The official preparations are Liquor calcis, lime-water; Syrupus calcis, syrup of lime; and Linimentum calcis, lime liniment, Carron oil. (See *Calcium.*)

CALX CHLORINATA.—Chlorinated lime, calx chlorata (U. S. P. 1890), commonly, but incorrectly, called chloride of lime. It is made by exposing slaked lime (calcium hydroxide) to chlorine gas. It is employed as a disinfectant and deodorant. (See under *Chlorine.*)

CALX SULPHURATA.—Sulphurated lime, commonly, but incorrectly, called sulphide of calcium, is a mixture of not less than sixty per cent. calcium sulphide with calcium sulphate and carbon. It is employed as an antiseptic and "alterative," and is credited with a curative and prophylactic action in suppurative processes, especially in furunculosis. Dose, gr. $\frac{1}{10}$–i. (0.006–0.06) in powder. Externally it is employed as an antiseptic in skin diseases, in the form of Vleminck's solution, Liquor calcis sulphuratæ (N. F.). (See under *Sulphides.*) T. L. S.

Calycanthus.—(Properly *Büttneria*). A genus of three species of shrubs in the family *Calycanthaceæ*, growing in the United States. The bark and leaves of *B. fertilis* (Walt.) Kearney, commonly known as the sweet-scented shrub or strawberry shrub, are used in domestic practice as an antiperiodic. The plant is chiefly of interest because of the poisonous nature of the seeds, sheep being killed by eating the fruit. An alkaloid, calycanthine, has been extracted by Dr. R. G. Eccles from these seeds.

H. H. RUSBY.

Cambogia.—GAMBOGE. "A gum resin obtained from *Garcinia hanburyi* Hook. f. (fam. *Hypericaceæ*)." (U. S. P.) This genus comprises about forty species of Eastern tropical evergreen trees with yellow juice. Other species yield the Mangosteen fruit and bark, and the Kokum butter. The gamboge tree is a native of Cambogia, Siam, and Cochin China, whence the supply of the gum resin for European and American consumption is obtained; but there are besides several other species of *Garcinia* in India, China, and the Asiatic islands, which supply similar products, if not exactly the same. Gamboge is collected by cutting or wounding the twigs or trunks, when the bright yellow latex flows slowly out, and is collected in vessels, usually bamboo joints, fastened at the lowest part of the incisions. Here it slowly hardens, or is perhaps dried over a fire, until a solid mass results, of the shape, usually cylindrical, of the containing vessel. The bamboo is then split off, and the gamboge is packed in large boxes for transportation.

That thus collected in bamboo joints is known as "pipe gamboge." Saigon, or "purse" gamboge, is collected in pockets of leaves or cloth, six or eight inches long by three or four broad. It is usually a little darker than the former. When run or massed into large blocks or tubs, it is called "cake gamboge," or "gamboge in sorts."

The pipe gamboge is preferred, not only because it represents the typical quality, but because it is almost invariably pure and clean. The large cakes are liable

to extensive adulteration with stones and pieces of iron. Being often formed in tubs or boxes, the gamboge is very apt to come into contact with nails or other metal, which turns it dark for a considerable distance from the offending body.

Gamboge has been used in China and India as a pigment for many centuries, and appeared as a purgative in Europe early in the seventeenth century. Its use in medicine, however, has always been insignificant in comparison with its consumption as a yellow paint, for which use it is hardly excelled by any pigment.

The best of that which reaches us is in cylindrical pieces, usually hollow at the center, two to five centimeters (1 to 2 in.) thick, longitudinally striate on the surface; fracture flattish-conchoidal, smooth, of a waxy luster, orange-red; inodorous; taste very acrid; powder bright yellow, sternutatory; free from starch.

Gamboge should yield not less than seventy per cent. of resin and not over three per cent. of ash.

It does not dissolve in water, but forms a very fine, smooth, yellow emulsion with it, and it is wholly soluble in potassa solution.

Gamboge contains about seventy-two (Christison) per cent. of yellow resin called *cambogic acid*, an orange-yellow, tasteless, and odorless mass, soluble in alcohol and ether, but not in water, having the purgative properties of gamboge, but less intensely than the crude gum resin itself. It also contains fifteen or more per cent. of *gum*, a little water, and some impurities. Its activity is proportional to the percentage of resin in it.

Action and Use.—This is one of the most violent of hydragogue cathartics, producing abundant watery stools and considerable griping, on which latter account it is not often now given alone, or for its full effect. It is, however, frequently added in small doses to the other cathartic combinations, and experience has proved its usefulness. It is especially valuable in such conditions as lead colic and seasickness, where the bowel requires powerful stimulation.

The full dose of gamboge is about 0.3 gram (gr. v.), but less is advisable in compositions; the maximum daily quantity, by the German Pharmacopœia is one gram. It is an ingredient in the compound cathartic pills (*Pilulæ Catharticæ Compositæ*, U. S. P.), each of which contains about a quarter of a grain.

H. H. Rusby.

Camden, S. C.—Situated in the pinewood, sandhill region of the State, about thirty miles from Columbia and twenty hours from New York. It is a town of about 3,500 inhabitants, between 150 and 200 feet above sea level, and has a mild sunny climate. The soil is very dry and porous, so that after a heavy shower the roads are not wet, the water quickly soaking into the sandy soil. The water supply and drainage are said to be good. The climate data are as follows:

Mean temperature (Fahrenheit): spring, 61.90°; summer, 79.32°; autumn, 62.26°; winter, 45.16°. Average annual rainfall for twenty years, 42.22 inches. The coldest noon temperature in February, 1890, was 50°; in March, 40°; in April, 50°. The warmest noon temperature was: in February, 83°; in March, 81°; in April, 86° (Solly). The prevailing winds are south and southwest. In February and March there are some high winds, but generally the air is remarkably soft, dry, and balmy. "Frosts occur at night only, and snow is exceptional." The exact number of sunny days is not known, but is said to be large. The relative humidity, though not known for this place, is probably not very different from that at Aiken, which is fifty-nine per cent. for December, January, and February.

The especial advantages claimed for this region as a health resort are "its dry, balmy, bracing air, with conditions favorable for constant out-of-door life"; its dry, sandy soil; the pines, and its easy accessibility.

Camden would appear to be a good resort for the open-air treatment of pulmonary tuberculosis, in its early stages, for cases not suitable for the colder regions or altitudes; also for convalescents from influenza, pneumonia or pleurisy, chronic bronchitis with much secretion, asthma, general debility, insomnia, and for those who merely desire to escape the dampness and cold of the Northern winter. The accommodations are good, there being both well-kept hotels and good private boarding-houses.

Edward O. Otis.

Cammidge Reaction.—This test was devised by P. J. Cammidge in an endeavor to discover in the urine some substance which should be indicative of pancreatic disease. The technique of the reaction as finally proposed is as follows:

The urine is freed from albumin (by heat and acetic acid) and from sugar (by fermentation) and filtered several times through the same paper. Forty c.c. of this clear filtrate are boiled for ten minutes with 2 c.c. strong hydrochloric acid (specific gravity 1.16) in a small flask with a funnel condenser. This is cooled and diluted up to 40 c.c. with cold water. Then eight grams of lead carbonate are added slowly, the liquid allowed to stand for a few minutes, cooled again in running water and filtered until perfectly clear. The filtrate is then shaken well with eight grams powdered tribasic lead acetate and filtered as clear as possible, the process being repeated several times if necessary. It is then shaken well with four grams powdered sodium sulphate, heated to the boiling-point, cooled in running water and filtered carefully. Ten c.c. of this perfectly clear transparent filtrate are diluted to 17 c.c. with distilled water and added to two grams sodium acetate, 0.8 gram phenylhydrazin hydrochloride, and 1 c.c. fifty-per-cent. acetic acid. This is boiled for ten minutes in a small flask with a funnel condenser, filtered while hot through paper moistened with hot water and the filtrate diluted to 15 c.c. with hot water if necessary. The crystals separate in a few hours in a characteristic reaction, but it may be necessary to leave the preparation over night before a deposit occurs.

From his own experience Cammidge was led to believe that the reaction was positive in the majority of cases of pancreatic disease and negative in other affections. As the observers multiplied, however, and the results of the application of the test accumulated, it became obvious that the claims of the author could not be substantiated. It was frequently positive in the urines of healthy individuals and often negative in those cases in which the pancreas was known to be diseased. In other instances the results would vary from positive to negative almost daily. In 1911 the explanation of these anomalous results was furnished by the work of Roper and Stillman. These authors were able to show that the so-called "typical crystals" were in fact an osazone of glycuronic acid and that the prescribed technique did not remove all of that acid from the urine. They were able repeatedly to obtain positive reactions in urine from patients suffering from constipation or who had received large doses of chloral, in both of which conditions the glycuronic acid excretion is increased. Their work was later confirmed in its entirety by Mayesima who arrived at practically the same conclusions. Mayesima's article contains also a fairly complete bibliography on the subject. As a result of this work the test has been accepted as indicating merely an increase in the conjoined glycuronates in the urine and therefore without diagnostic value in pancreatic disease. Its use has been almost completely discontinued.

Ralph G. Stillman.

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Campanulaceæ.—(The Harebell or Lobelia Family.) This family, of some two score genera and more than a thousand species, is of greater interest through its poisonous species than through its medicinal value. Its plants represent every habit, though the most of them are herbs and there are no large trees among them. The juice is milky and the flowers are mostly showy. They inhabit all except very cold countries. Of the three subfamilies, the first, *Campanuloidæ*, is much more closely related, in composition and properties, to the distinct family *Cichoriaceæ* than to the remainder of its own family, and it appears, from various considerations, to be a mistake to class these and the third subfamily, *Lobelioidæ*, in the same family. The Campanuloidæ are not poisonous, but, on the contrary, produce numerous wholesome and nutritious roots, containing inulin, and some of their fruits also are edible. Of the *Lobelioidæ*, on the other hand, one or more species will be found recognized in almost every country as deadly poisons. The poisonous constituents are chiefly alkaloids. As poisons, they are classed as acrid narcotics, and act generally like *Lobelia inflata*, which see.

Henry H. Rusby.

Camphoid is a substitute for collodion made by dissolving 1 part of soluble gun cotton (pyroxylon) in alcohol containing 20 parts of camphor. It is a thick, colorless liquid which dries very rapidly, and when painted on the skin leaves a thin impervious film. It may be applied as protective, or a vehicle for iodoform, chrysarobin, tannic acid, etc.

W. A. Bastedo.

Camphor.—*Camphora.* The dextrogyre modification of the saturated ketone ($C_9H_{16}CO$) obtained from *Cinnamomum camphora* (Linné) Ness et Ebermaier. (Fam. *Lauraceæ*) and purified by sublimation. The camphor plant is a large tree of slender habit, with long, horizontal, smooth, green branches, and a hard, light-colored, very fragrant and valuable wood. The alternate evergreen leaves are dark and shining above, lighter, glaucous-green beneath, ovate acuminate, entire, three-nerved. Flowers minute, greenish-yellow, in small axillary panicles. This tree grows extensively and abundantly in Formosa and the Japanese islands, from which places most of the world's supply, about ten million pounds, is derived. It has also been transplanted and flourishes in most tropical or subtropical countries of both hemispheres.

There are a number of other and non-official camphors. The best known are the Borneo and Ngai camphors. The former is collected on the islands of Borneo and Sumatra from *Dryobalanops camphora*, the latter from *Blumea balsamifera*, which grows abundantly throughout China and India. The increasing demand for camphor in the arts, particularly in the manufacture of celluloid is directing attention to its production, as the demand is exceeding the natural supply. To replace this deficiency the manufacture of artificial camphor has been developed, with some measure of success. A more important measure has been the planting in Formosa, by the Japanese government, of many millions of trees.

Camphor is an oxidation product of the essential oil of camphor, which is abundantly present in all parts of the plant. Very frequently it is found in a more or less pure state beneath the bark, having separated from the oil.

Camphor occurs "in white, translucent masses, of a tough consistence and a crystalline structure, readily pulverizable in the presence of a little alcohol, ether, or chloroform; having a penetrating, characteristic odor, and a pungently aromatic taste. Specific gravity, 0.995 at 15° C. Very sparingly soluble in water, but readily soluble in alcohol, ether, chloroform, carbon disulphide, benzin, and in fixed and volatile oils. It melts at 175° C., boils at 204° C., and is inflammable, burning with luminous, smoky flame. On exposure to the air it evaporates more or less rapidly at ordinary temperature, and, when moderately heated, it sublimes without leaving a residue." (U. S. P.) The solubility of camphor in water is about one part in 1,300; this is increased by the presence of sugar, magnesia, carbonic dioxide, and spirit of nitrous ether.

Fig. 1187.—Camphor Tree, Flowering Branch. (Baillon.)

Camphor is absorbed from the skin and mucous membrane, and is found unchanged in the blood and the various organs and tissues. The kidneys do not excrete it unchanged, but it is thought to be excreted by the lungs and skin. In its action camphor is antiseptic and stimulant, with a sedative effect following the primary stimulation. This action is exercised upon the surface when applied externally, and when administered internally, the same effect is directed to the mucous surfaces with which it comes in contact. It is particularly comforting in "day-cough," and when the sense of suffocation is marked. In the stomach it stimulates the muscular coats, adds a sense of warmth, and reflexly stimulates the heart and abdominal circulation. After absorption its action is directed to the cerebral and spinal centers through which it influences the heart and vascular system.

Camphor is not now employed therapeutically to the extent that it was formerly. It is of value in cardiac and circulatory depression, and in all conditions in which rapid stimulation is required; as in typhoid conditions, pneumonia, edema of the lungs, and dilatation of the heart. In chronic depression of the nervous system when there is a loss of control it is a useful stimulant in repeated small doses. Hysteria, chorea, epilepsy, spermatorrhea, and melancholia are some of the conditions in which it has been employed. Its excretion by the skin and bronchial mucous membrane has made it a very useful diaphoretic and expectorant, and in febrile states, particularly when combined with opium and other diaphoretics, it has always been recognized as of much service. Its action upon the genitourinary organs has been a disputed point. It is supposed to have a sedative action and also to possess anaphrodisiac properties. After its continued use it certainly acts an as anaphrodisiac. As a

sedative it is combined with bromides, opium, and hyoscyamus.

In large doses camphor excites the brain and produces a form of intoxication. Its continued use produces a craving for the drug, and it has been shown that a camphor habit may be acquired.

The dose of camphor is gr. j.–v. (0.06–0.3). It may be administered hypodermically, particularly in conditions of collapse. For this purpose a ten per cent. solution in oil is used. It may be given in pills or capsules, or in powder with sugar, or the spirit of camphor may be given in wine. The camphor may also be dissolved in ether and added to wine. The following forms a good emulsion: camphor, gr. xv.; ol. olivæ, ʒij.; mucil. acaciæ, ʒv.; syr. simplicis, ʒi.

Monobromated Camphor ($C_{10}H_{15}BrO$).—This is a substitution compound of camphor in which one atom of hydrogen is replaced by one of bromine. It is official in the United States Pharmacopœia. It occurs in colorless prisms, with a taste and odor of camphor. It is almost insoluble in water, but soluble in alcohol and fixed oils. It is permanent in the air and unaffected by light. This compound was introduced as a nervous sedative and antispasmodic. It is employed as a cardiac sedative, in hysteria and other nervous affections, and for the relief of undue sexual excitement. It has also been used as an hypnotic. The dose is from gr. i.–v. (0.06–0.3). When its administration is being pushed its effect requires to be watched, as when given in excessive doses to animals it produces muscular weakness, paralyses, and depression of the vital centers. On account of its disagreeable taste it is administered in pill form, in capsules, or in tablet triturates.

Camphor Oil.—The oil of camphor of commerce is separated during the first sublimation and is obtained as a thin fluid, varying in color from a light yellow to a reddish-brown according to age. It has a strong odor and taste resembling those of camphor. It is very variable in character, the percentage of camphor that may be present is uncertain, some samples being entirely free from it. The oil is not of much therapeutic value in this country, although thought much of in China and other Eastern countries, where it is employed not only for its remedial properties but also as a turpentine in the preparation of india ink and varnishes. It is also used as an illuminant. Its action is similar to that of camphor, and it is recommended in the same conditions in doses of ♏ i.–iii. (0.06–0.2).

Camphoric Acid ($C_{10}H_{10}O_4$).—This is an oxidation product of camphor, and may be prepared by heating camphor with nitric acid. The acid forms in small colorless needles or plates, odor faintly aromatic, taste acid and bitter, very sparingly soluble in cold water, more soluble in hot, soluble in alcohol and ether. Ten per cent. of alcohol added to hot aqueous solution prevents the acid from being deposited on cooling. This acid has long been known, but it is only during the last few years that its therapeutic properties have been utilized. Its chief use is in the treatment of diseases of the respiratory tract and as a preventive of night sweats. For the latter purpose it is one of the most valuable additions to our materia medica.

The dose as an anhidrotic is gr. xxx. (2.0) at bedtime, or gr. xv. (1.0) during the afternoon and the same dose repeated at bedtime. The action is not rapid, and in some instances no effect has been noticed until the following day. The effect of a single dose often continues for several days. It does not in any way interfere with the appetite or digestion, and in most instances a quiet sleep follows its use. As the taste is somewhat disagreeable, it is best administered in wafers or capsules.

In diseases of the mucous membrane of the respiratory tract, comphoric acid is used by applying locally and as a spray. In acute coryza, pharyngitis, and laryngitis, a half- to one-per-cent. solution may be used every three hours, or tampons saturated in the solution may be introduced into the nasal cavities; in ulcerated throat, a solution of two to six per cent. may be applied.

Internally, it is also used for catarrhal diarrhea and when intestinal antisepsis is desired, the dose being from gr. v. to gr. xv. (0.3–1.0). It is excreted by the kidneys and renders the urine clear and acid in two or three hours.

In cystitis, when the urine is alkaline, it has proved of benefit. In this condition it is also used as a wash in a half of one-per-cent. solution. The bladder is to be irrigated twice a day, about an ounce of the solution being left behind. Beaumont Small.

Camphor Salicylate.—This is a compound of eighty-four parts of camphor with sixty-five parts of salicylic acid. It occurs as a crystalline, camphor-like mass, or it may be made to crystallize out from its solution in benzol. It is insoluble in water and glycerin, soluble in alcohol, in mineral oils, and in twenty parts of olive oil. Used internally as an intestinal antiseptic and carminative, it acts in the alimentary tract like salol. Its systemic effect, however, is not marked, and its internal use has up to the present been confined mostly to the summer diarrheas. The dose is gr. i. to v. (0.06–0.3). In lupus and other skin diseases it is applied locally in the form of an ointment or liniment of from five- to twenty-per-cent. strength. W. A. Bastedo.

Camps, Hygiene of.—See *Military Hygiene.*

Camptodactyly.—An affection first described and named by Landouzy in 1885. Meaning literally "bent fingers" it denotes an acquired deformity and not, as its name might suggest to some, a congenital malformation, The same name has also been given to another acquired deformity seen in connection with Heberden's nodes, and might readily be applied to various affections secondary to diseases of the joints and aponeuroses, tendons, muscles, etc. It is therefore important to determine whether there really exists an independent primary affection which is in no wise affiliated with others already known. This task is by no means simple, for some of the most characteristic cases of camptodactyly have been described in connection with certain well-known arthropathies. It seems certain, however, that this association represented a pure coincidence.

Our knowledge of this affection is based largely upon the thesis of H. Crepin (Paris, 1908), who analyzed 100 cases selected according to Landouzy's criteria. In two-thirds of this number the deformity was bilateral. In the unilateral cases the right hand was affected more frequently than the left in the proportion of about 3 to 2.

In seventy-six patients but one finger of a hand was affected—nearly always the little finger. In twenty-four patients more than one finger of a hand was involved—either the third or middle finger, one or both, in addition to the little finger. Only rarely was the index finger involved.

Let us now consider the character of the deformity. When the open hand is placed palm downward on a flat surface, the affected finger is seen to be bent after one of three fashions, according as the condition affects one or both of the two interphalangeal joints. In the first type there is a marked flexion, amounting in certain cases to as much as 90° at the proximal interphalangeal joint, the distal articulation being normal. In the second type, with both articulations flexed, the deformed finger assumes the shape of a hook. Finally, in the third type, the proximal articu-

lation is flexed and the distal one extended. This latter type was seen in twelve of the cases collected by Crepin.

Pathognomonic of camptodactyly is the absolute irreducibility of the deformity. The bent finger cannot be straightened, although it may be bent to a further degree. The patient does not appear to be incapacitated in any way, and there are even patients so unobservant as to be unaware of their deformity. There are no sensory disturbances, nor collections of fluid in or about the articulations.

Landouzy, who had the opportunity of studying the diseased articulations histologically, stated that the condition represents a minimal sclerosis of the fibrous capsule of the joints. The articular surfaces and synovial membranes are absolutely intact. The etiology and pathogenesis are so obscure that they can be approximated only by enumeration of certain predominances. Women are affected much more frequently than men, and the elements of actual traumatism and professional overuse may almost be neglected. A few well-marked cases have occurred in young children, while the majority supervene during youth as if the affection were largely developmental. Of great significance is the very frequent association of scrofulous and tuberculous accidents in the stock from which the patients are derived. In not a few cases the lesions coexist with pulmonary tuberculosis; also, however, with non-tuberculous chronic affections of the chest. This coincidence calls to mind that other deformity of the fingers known as pulmonary osteoarthropathy, which, however, seems quite distinct throughout from camptodactyly.

Another element which has often been seen to coexist with the latter affection is vasomotor in character, such as is responsible for the so-called acronoses. These include cyanosis and hyperidrosis of the digits. But like the ordinary phenomena of arthritism which sometimes coexist, this may be the result of pure coincidence. We may feel certain, however, that the eighty-seven per cent. of associated tuberculosis already mentioned is highly significant, so that camptodactyly may almost be regarded as a paratuberculosis of the joint capsules. From this viewpoint any associated arthritis in a tuberculous subject might be reckoned under Poncet's tuberculous rheumatism. The tuberculous factor makes the presence of camptodactyly in a young subject of considerable prognostic significance. In the old it may point to the possibility of a healed tuberculosis.

The silence of Crepin concerning treatment is intelligible when we bear in mind the essential refractoriness of the affection in connection with the absence of functional disability. EDWARD PREBLE.

Canada Balsam.—*Balsam of Fir.* The liquid oleoresin obtained from lacunæ in the bark of *Abies balsamea* (L.) Miller. This fine, tall tree is abundant in the Northeastern United States, northward and northwestward. Its leaves are much in demand for making "balsam pillows," which are deliciously fragrant. Its buds are often sold as balm of Gilead buds, but this name properly applies to those of *Populus candicans*. The oleoresin is collected by breaking the blisters upon the bark and catching the exudation. It is of a pale-yellow color, absolutely clear and transparent, somewhat viscid, aromatic, and bitter. It is insoluble in alcohol and water, but dissolves in ether and chloroform. It possesses the ordinary stimulant antiseptic and expectorant properties of the family (see *Coniferæ*), and is given in doses of gr. v. to xxx. (0.3–2.0). It is more largely used in microscopical mounting than otherwise, for which its perfect transparency peculiarly fits it.

HENRY H. RUSBY.

Canadian Hemp.—See *Apocynum.*

Canadian Medical Association.—This association was founded at a meeting of the profession at Quebec in 1867, under the presidency of the late Dr. Bayard of St. John's, N. B. For a number of years it met annually for the reading and discussion of papers and such other matters as might arise pertaining to the profession; but no systematic organization upon modern principles was made until 1900, when an up to date constitution was adopted. Incorporation by the Dominion Government was obtained in 1910. In 1911 *The Canadian Medical Association Journal* was established and is published monthly.

The management is in the hands of the Executive Council. This is formed of fifteen members elected at the annual meeting and delegates from the affiliated provincial associations: one for the first fifty members, one for the succeeding hundred and fifty, one for an additional hundred and fifty, and one for each three hundred members after that number. The Executive Council elects from among its members a Finance Committee of five who carry on the work during the year.

Any legally qualified regular practitioner is eligible for membership. The annual fee is five dollars, which includes a subscription to the *Journal.*

The meetings are held in the various Canadian cities. The president is selected from the province in which the meeting is held, and the Provinical Association merges its meeting with that of the parent association. BEAUMONT SMALL.

Canary Islands.—These islands, justly celebrated for their admirable climate and beautiful scenery, lie between the 27th and 28th north parallels of latitude, five degrees north of the tropics, and in longitude 13° to 18° W. They are in about the same latitude as Florida, Southern California, Southern Texas, Northern Egypt, and the Desert of Sahara. They are from 120 to 170 miles distant from Africa, and may be reached by steamer from Plymouth or Southampton, England, in from five to eight days; and from Cadiz, Lisbon, Gibraltar, Marseilles, or Genoa, in three or more days. The islands (of volcanic origin) are seven in number; but the two generally visited by invalids and always meant when the Canary Islands are referred to, are Tenerife and Gran Canaria, about thirty miles from each other. In these islands Las Palmas in Gran Canaria, and Orotava in Tenerife are the towns usually resorted to. The climate is characterized by medium dryness, a large amount of sunshine, equableness, and a stimulating quality; in brief, it is a moderately dry marine climate. "The Canaries lie in the region of the dry, northerly trade winds, which are the prevailing winds throughout the year, usually blowing about 240 days out of the 365, but more strongly and almost without break during the summer months; hence the mean maximum temperature of the summer months, which is about 77°, is lower than might be expected for the latitude" (Melland).

As both Tenerife and Gran Canaria are mountainous, the mountains rising to the height of 6,000 feet or more, there is both a shore and a mountain climate. For the summer, Melland considers the mountain climate superior to that of the shore in the treatment of lung diseases and already hotels adapted for invalids have been erected in these higher regions. During the winter months Las Palmas, of which Melland especially writes, is to be preferred, he says, for cases of early phthisis and rheumatism, to some of the other health resorts of the island, on account of the clear sky, free radiation, and abundance of sunlight. These advantages of Las Palmas are due to its geographical position away from mountains and northern slopes. The vegetation of these islands is rich and varied; the date, palm, pepper,

and eucalyptus are some of the trees found there; and of fruits there are oranges, apples, pears, peaches, plums, figs, grapes, guavas, bananas, pomegranates, and prickly pears. The flora is very extensive and the variety of plants great. "Anything put into the ground will grow," says Mrs. Stone.

The meteorological observations, taken at Las Palmas, are given by Melland as follows:

1889–93	Shade temperatures. Mean maximum.	Mean minimum.	Mean.	Range.	Bright sunshine, hours per diem	Rain, inches	Relative humidity per cent	Number of days any rain fell.
					Hrs. Min			
October...	73.4	65.8	69.6	7.6	5 30	3.22	73	7
November..	71.3	62.3	66.8	9	5 38	1.87	68.5	10
December..	67.6	57.2	62.7	9.7	4 50	1.86	68	12
January....	66.5	57.3	61.7	8.8	5 3	1.41	66 6	8 5
February..	66.5	55.7	61.2	10.7	6 9	.51	65.8	3.5
March..	67.4	56.5	62.1	11.2	5 57	.84	67.6	5
April.	69.3	59.1	64.2	10.2	6 23	.34	67.3	4.5
May.	69.2	61.3	65.4	8.4	6 43	.38	67	4
Average for winter.	68.5	58.8	63.6	9.7	5 41	8 15*	67.1	49*

* Total.

The small diurnal range of temperature is to be especially noted, as well as the slight variations from one month to another. The rainfall is very inconsiderable, and there is the small number of forty-nine days upon which any rain fell. Each day gave an average of over five hours and a half of sunshine. The relative humidity greatly decreases as one ascends into the mountain regions.

The following observations for Orotava are condensed from various observers:

Months of winter,	Average temperature, degrees.	Mean daily range, degrees.	Daily sunshine, hours per diem.	Relative humidity, per cent.
			Hrs. Min.	
November.	66.97	11.8	.....	67.3
December.	65.05	11.2	5 48	63.2
January...	62.88	11.2	5 42	61.5
February..	61.1	12.1	5 47	68.6
March...	62.7	11.9	7 32	66.9
Average for winter.	63.74	11.6	6 12	65.5

The temperature of Orotava, says Gihon (Transactions of the American Climatological Association, 1889), never falls below 50° F. or rises above 82° F., and attains these extremes only on rare occasions.

"The February of Orotava," continues the same writer, "is the June of London, the May of Paris, and the April of Rome, Nice, and Cannes." In Orotava storms are unknown, and linen garments may be worn the entire year. "Here, if anywhere," to again quote Gihon, "reigns perpetual spring, without fogs and frosts, where the sap never dies, where rain seldom falls, winds and storm are scarcely known, and burning heat is never felt."

From observations taken at Las Palmas, it is seen that the six warmest months are from June to November, with a mean temperature of 71.7° F.; and that the six coldest months are from December to May, with a mean temperature of 63.5° F. September and October are the hottest months, with a mean temperature of 73.5° F.; but they differ from the coldest month, February, by only 13.5° F.

The mountain climate of the Canaries, at an altitude of from 1,300 to 5,000 feet, differs from that on the coast by increased dryness—the relative humidity at the village of Villa Flor (4,300 feet) for the month of August being thirty-five per cent.; by the absence of the northerly trade winds; by the absence of rain during the summer; by a greater range of temperature; by a more invigorating atmosphere; and by almost continuous blue skies. The summer is the proper season for visiting the highlands, as the climate is then at its best. "Here," says Brown ("Madeira and the Canary Islands," by A. Lander Brown, London, 1896), "the invalid may live for months under a rainless blue sky and in a genial climate, wandering among gorgeous forests and magnificent precipices; below him a vast sea of billowy cloud out of which the summits of the other islands rise, beckoning him to new explorations." Melland considers the mountain climate much more rapidly curative in cases of early phthisis than that of the coast. In some of the mountain stations, as at Laguna (1,800 feet) in Tenerife, there are good accommodations, and camping is also a not infrequent method of living in the higher altitudes. Orotava consists of the town, or Villa de la Orotava, at an altitude of 1,100 feet, and three miles distant from this is the Puerto de la Orotava on the coast; it is the latter locality to which invalids resort. Round about these two Orotavas and including them is the famous Orotava valley, which Humboldt considers "the loveliest scene in the world," and of which M. J. Leclercq, in the *Annuaire du Club Alpin Française*, 1879, writes: "I have seen sights more varied, more striking, and a more brilliant sky; vegetation is more thoroughly green in the celebrated Cintra Valley in Portugal, which Bryon considered the most delicious locality in Europe; but where can be found those mountains and classic beauty, those velvety tints, that soft and balmy atmosphere, that moderate temperature, notwithstanding the vicinity of the torrid zone, that charm impossible to define?"

And of its climate W. Vignal writes (*British Medical Journal*, 1893): "I do not think it possible to find anywhere a more perfect climate, and as far as I know there is none comparable to it."

From May to August there is no rainfall at Orotava, and the annual precipitation is thirteen inches. The average number of rainy days is fifty-one; and the rain falls most frequently at night. The temperature of sea water is lowest in March, 64°; and highest in July, 68° (Solly, "Medical Climatology").

In comparing the Canaries with Madeira, the former have in common with the latter the equability of climate, but they have a slightly higher temperature and are considerably drier, the relative humidity from November to April at Orotava being 64.9 per cent., and at Funchal, Madeira, during the same time, 72 per cent. The Canaries, say Weber and Foster, "have a greater claim as health resorts than Madeira and offer good accommodations, but are much wanting in means of amusement." The accommodations at Las Palmas and Orotava, and at some of the other towns in the islands, are good and abundant. The water-supply at Las Palmas and Orotava is brought from the mountain, and is of good quality. There is no general drainage system, but each hotel has its own private water drainage system; in general, cesspools prevail. The soil is porous and dries rapidly after rain. Zymotic diseases are not common. At Las Palmas quite recently a cold-storage and freezing establishment has been opened, and a building estate developed, with villas suitable for residents and visitors. At present most of the invalids and visitors come from England.

The diseases for which the climate of the Canaries is favorable are incipient phthisis for an arrest, and advanced phthisis for alleviation, in cases of feeble

nutritive power. As Huggard so well puts it, "the climate that makes that demand on the assimilative powers generally to which the organism can best respond is that which will secure the highest resistive power to tubercular disease, be it a cold or a warm climate." Las Palmas or the port of Orotava in the winter, and the mountains in the summer—scrofula, chronic bronchitis, heart diseases and Bright's disease, and rheumatism.

While we have a climate in many respects similar to that of the Canaries, in Southern California, more especially inland, and in some portions of the Southwest, the novelty of the change, the ocean voyage, and the variety and beauty of the scenery of the "fortunate isles" may tempt some invalids to try its mild, sunny climate and pure atmosphere, and enjoy the "*equability* of an island climate combined with the *dryness* of a continental one."

For a more extended account of the Canaries the reader is referred to: "Tenerife and Its Six Satellites," by Olivia M. Stone, 1887; "Madeira and the Canary Islands," by A. Lander Brown, 1896; "The Canaries for Consumptives," by E. Paget Thurstan, 1889; "Climatic Treatment in Grand Canary," by Brian Melland, in *The Medical Chronicle*, Manchester, England, 1897; "The Canary Islands as a Health Resort," by John Whitford, 1890; "The Therapy of Ocean Climate," by Albert H. Gihon, M. D.; in the Transactions of the American Climatological Association, 1889; "Madeira and the Canary Islands," fifth edition, 1898, by Samler Brown; Huggard, "Handbook of Climatic Treatment," 1906.

EDWARD O. OTIS.

Cancer, General Etiology, Diagnosis, and Treatment.—For the purposes of this discussion "cancer" will be taken to mean malignant tumor and not necessarily a malignant tumor of epithelial origin. Many of the characteristics common to all malignant tumors are more important than the differences between them depending upon the different histological structure of the tissues comprising them. Moreover, certain facts about malignant tumors of non-epithelial type throw light upon the life history of cancers of epithelial origin. In one sense, therefore, the popular definition of cancer, that is, a malignant tumor, is the best one. But of course, this definition does not really define—for what is "tumor?"

At one time tumor meant any unusual swelling and the term is still used in this general sense by medical writers, especially those using the German language. Gradually, however, the tendency has been to restrict the meaning of the word. In the first place, the increase in bulk of any part of the body, due to the displacement of natural parts as exemplified by herniæ of all sorts, have been excluded. The same fate followed such masses as are produced by the accumulation and "backing up" of any glandular secretion leading to increase in the size of the gland affected or of the reservoir provided for storage of the secretion. As examples of such masses may be named the swollen parotid gland in the obstruction of its duct, an enlarged gall-bladder, and, if excretions be considered, an overdistended urinary bladder. More difficult differentiation attended the analysis of such increase in volume as is dependent upon inflammation; this is attended with real increase of tissue, and increase of tissue has always been looked upon as one of the earmarks of tumors. However, it soon became evident that such swellings must likewise be excluded: they frequently receded as soon as inflammation was over; they were easily affected by various mechanical and chemical therapeutic procedures; furthermore, the light thrown upon them by the progress in our knowledge of infectious disease showed that in numerous instances the real excitants of these swellings could be isolated and could be made to produce similar swellings in animals. In cases where such isolation has so far been impossible, analogy justifies us in thinking that similar excitants of disease may be present but have yet escaped discovery because of the limitation of our physical means of investigation. Finally, numerous instances of physiological and pathological hypertrophy have been excluded from our consideration of tumor; for example, the pregnant uterus, the hypertrophied heart, the enlarged thyroid gland, the functionating breast.

All these then are not tumors. The latter cannot be defined at the present state of our knowledge of them, but they may be described as persistent masses of atypical and newly formed tissue, of unknown etiology, usually developed from a single starting-point; independent of the general purposes of the organism of which they are part, and therefore subserving no useful function; capable to a great degree of increasing in size at the expense of the surrounding structures and of the body welfare in general.

This description is certainly imperfect and its imperfections are due to our ignorance of the causes of tumors. The difficulty is perhaps best illustrated by considering the history of tuberculosis. The many descriptions characterizing this disease went by the board as soon as its infectious nature and its excitant were demonstrated. Tuberculosis now simply means the phenomena caused by the lodgment and growth of tubercle bacilli in the organism together with the consequences of such growth. This definition is ample and exclusive and there is no necessity for recounting what the phenomena of tuberculosis are; they differ with the localization of infection, with the age and condition of the patient, with the duration of the disease and finally with the treatment pursued. Tumors, on the other hand, are known to us only by their phenomena and there is no unifying factor such as a common etiology to group these conditions under a simple definition. For all we know the phenomena which we call cancer disease—*die Krebskrankheit* of the Germans—are really common to different conditions and there may be cancer diseases as different from each other as chancroid and chancre, for instance, which at one time were likewise gathered in one group of venereal sores.

Malignancy distinguishes cancers from other tumors and the term must not be confounded with the mere gravity of the affection so far as prognosis is concerned. The latter depends very much upon the site of the tumor and not merely upon its character. A perfectly benign tumor may mean speedy death to the patient if it is situated in the brain, for instance, and is not accessible to operation. Tumors of whatever character pressing upon the respiratory passages may likewise be of very grave import. On the other hand, a malignant tumor like epithelioma may spread so slowly as to be quite compatible with good health and fair comfort of the patient for many years. Williams names the following characteristics of malignancy: (1) Persistence, with a tendency to softening and necrosis; (2) an infiltrating mode of growth so that the margin of the tumor interpenetrates and destroys the surrounding structures; (3) dissemination, by which is meant the power of the primary tumor to form secondary tumors like itself: (*a*) in the vicinity of the primary tumor, (*b*) in the adjacent lymph glands, etc., (*c*) in distant parts of the body, such as the liver, lungs, bones, etc.; (4) recurrence, or the power of the tumor to grow again, even after the most drastic attempts to ensure its complete destruction by the knife, fire, caustics, etc.; and (5) cachexia, or a certain impairment of the general health with wasting. A few remarks upon the etiology of cancer must precede the discussion of these clinical phenomena of the disease.

SPECIAL ETIOLOGY.—The special etiology of cancer is closely bound with etiology of tumors in general

and is not within the limits of the present discussion (see article Tumors, in this Handbook). Here it need only be stated that the various theories regarding the causation of cancer may be gathered under two general headings: the parasitic theories, and the theories of cell autonomy. It has been abundantly proved that *parasites* may have a certain etiological relation to cancer; inflammatory reaction produced by them has frequently enough been seen to pass on into malignant disease. But neither bacteria, yeasts, nor protozoa of any nature have been proved to be the immediate excitants of malignant disease, and it is almost unquestioned that, whatever the primary causative agent, the growth of cancer and the phenomena of cancer are due to the multiplication of *cancer cells*. Any assumed parasite must have more intimate relations to these cells than any microorganism known to us at the present time.

The theory of *cell autonomy* assumes that cancer cells are simply tissue cells that have thrown off the subtle control of the organism, which must be active in every physiological cell or group of cells, and have assumed the unlimited capacity for growth which characterizes embryonal cells. In the present state of the theory, Cohnheim's hypothesis of embryonal rests, Ribbert's of misplaced adult cells, etc., are looked upon as only partial truths, for while numerous cases of cancer may be explained by these assumptions, the great majority do not need them to explain the limitless capacity for growth of their constituent cells. That property is inherent in the cells of the organism, and the development of cancer is due not to any newly assumed character, but rather to an "open" assertion of latent powers. It may be stated that the theory of cell autonomy has found most supporters among laboratory workers, men who are supposedly most conversant with the properties of animal cells and tissues. In one sense it is a less hopeful theory, for it means that the problem of cancer is really the problem of life and growth of tissues in general and our knowledge of that subject is still in its infancy. The theory of cancer parasite, on the other hand, leaves open the possibility of the discovery of such a parasite either as a result of chance or as a result of the fairly complete methods that have been developed with the growth of our knowledge of infectious disease. Fair consideration, however, shows that the theory of cell autonomy explains and unifies the various apparently conflicting clinical and pathological phenomena of cancer better than any other assumption, and it therefore should be accepted as a working hypothesis; such consideration may save in the future the laborious efforts made by numerous investigators in the past who could see no other cause for cancer but a special cancer parasite.

While the renewed interest in cancer research has not been rewarded by the discovery of a cause for cancer, numerous points in the etiology of malignant disease have been recently elucidated and we shall now turn to their consideration.

Increase of Cancer.—Everybody is conversant with the fact that the last few decades have witnessed a remarkable decrease in deaths from infectious diseases and from affections of infancy, while on the other hand the degenerative diseases of the heart, arteries, kidneys, and the nervous system, as well as a few of the diseases of metabolism have increased in incidence. At first sight it would seem easy to decide whether cancer is likewise on the increase but a consideration of the many points of difference between statistics of cancer several decades ago and at present leads us to grant that while increase in cancer has *probably* taken place, the support of such conclusion is far from amounting to very strong proof.

Autopsy statistics have almost everywhere shown an increase in the relative number of cancer autopsies as compared to the total number of cases. Buday gives the following table:

Statistics of	Year or period.	Percentage of cancer-bodies to total number.	Remarks.
Orth, Berlin	1875 1885 1907	4.9 7.0 14.11	Percentage of total number of bodies.
Lex (Heidelberg).	1870–1879 1900–1907	6.37 9.13	Percentage of total number of bodies.
Beck, Munich	1874–1884 1894–1904	7.0 12.5	Percentage of bodies of persons over 15 years old.
Steinhaus (Brussels).	1888–1897 1898–1907	8.6 9.07	Percentage of bodies of persons over 20 years old.
Feilchenfeld..... Redlich.....	1895–1900 1900–1905	13.24 13.00	Percentage of bodies of persons over 20 years old.
Buday (Kolozvar).	1870–1888 1889–1905	8.0 9.91	Percentage of bodies of persons over 20 years old.

Thus it is seen that with the exception of Redlich's figures which show a small drop, most of the statistics show a well marked rise in the percentage of bodies with cancer coming to autopsy. But the rise in figures could well be explained by the fact that cancer patients are much more apt to seek treatment in the hospitals nowadays than a few years ago. Orth, however, thinks that even if every allowance is made, the autopsy statistics show a moderate increase in incidence of cancer.

General mortality figures give a somewhat similar picture. In the United States the mortality from cancer per 100,000 living increased from 9 in 1850, to 29 in 1880, to 33 in 1890, and to 43 in 1900. The absolute figure of deaths for 1909 as given by the incomplete reports of the census of 1910 is in round numbers 75,000, which shows an increase of about 8,000 over the mortality in 1908. In the year 1909, cancer stood the sixth in the list among the causes of death, tuberculosis, pneumonia (all kinds), heart disease, nephritis, diarrhea and enteritis being the only causes exceeding the toll claimed by malignant disease.

The mortality statistics in England show that in 1840, the cancer death rate per million living was 177; in 1870, 424; in 1890, 828; in 1905, 885 (Williams). Statistics of other lands show similar increases, except that such increases do not appear to be as great in the last few years as in previous decades. This is especially true of Denmark and Switzerland, in which increase in cancer mortality just about keeps even with general increase in population. This fact is noteworthy as these two countries have paid careful attention to the correctness of their statistical publications.

There are many who consider that any such increase as seems apparent from the above is well explained by the great saving of life because of diminution of deaths in infancy, and at any age, from infectious diseases, so that more persons now reach the "cancer age"; because of the increased correctness of diagnoses; because of better kept mortality statistics in almost all lands. Williams states, however, that the saving of life is true only of precancerous age; that the diagnosis of cancer early in its development may be difficult, but it is not very hard to recognize it later and as a cause of death; that improved statistics have likewise diminished supposed "cancer" deaths by excluding

various indefinite terms as fibroid, polypus, etc., which previously were included under cancer.

W. B. Coley thinks likewise that any attempts to explain away increase of cancer are far from convincing. He thinks that actual deaths from cancer are much higher than the reported deaths, because of the strong prejudice against the word "cancer" among laymen, which leads physicians to name intercurrent affections, etc., as causes of death in cancer patients. In the United States, statistics of "inaccessible cancer," which should show most increase because of improvement in diagnosis, show relatively less increase than deaths from easily diagnosed causes. In the period 1868 to 1888 deaths from cancer of the stomach increased 22 per cent. in males and 44 per cent. in females, while in the same period the death rate from cancer in general went up 50 per cent. He states that the death rate from cancer is rapidly approaching that of tuberculosis.

It may be hoped that the next few years will see this controversy settled, for the later governmental statistics are fairly uniform and therefore comparable, while the other modifying factors, better diagnoses, decreased mortality in youth, etc., will have been fairly stationary in their effects. Meanwhile, it would seem that the weight of evidence is on the side of those who claim that a moderate increase in cancer has been gradually taking place.

Age.—C. P. White has analyzed 4,125 cases of cancer, observed in the General Hospitals of London, with reference to the influence of age on the incidence of cancer. Such figures, of course, do not give the incidence of the disease in the community in general. On the other hand, they are free from gross errors, due to mistakes in diagnosis and to incomplete statements in death certificates which frequently name a fatal intercurrent affection without naming coexisting cancer and fail to separate sarcomata from carcinomata. The latter point is important as the age relations of the two varieties of cancer are very different. Of the cases analyzed, 1,928 were in male patients and 2,197 in female patients. Curves based on these figures show a rise in the incidence of carcinoma at about the age of twenty-five; this is followed by a slow and then a more rapid climb, the maximum being reached at fifty in the females and at fifty-five in the males. After the latter age a rapid descent takes place.

On the other hand, 907 cases of sarcoma, of which 516 were in male and 391 in female patients, analyzed in the same manner, show quite a different result. The curve of incidence starts at a fairly high point because of the frequency of congenital tumors and of tumors of early life of sarcomatous nature. It drops rapidly during the first half of the second decade of life, and then rises during the period of adolescence. From that time on it remains high with moderate fluctuations, and finally descends rapidly after the fifth decade of life is passed. The high starting-point, that is, the great number of congenital tumors, may be erroneous, according to White, because of the many teratomatous and mixed tumors diagnosed as sarcomata.

Williams quotes the general mortality figures in England and Wales for the year 1900 which show that the maximum mortality from cancer is attained for both sexes during the decennium fifty-five to sixty-five; ninety-five per cent. of the total deaths occurring after the thirty-fifth year, and eighty-six per cent. after the forty-fifth year. He remarks, however, that such age distribution cannot be regarded as anything characteristic of cancer for a similar tendency is present with many other diseases because of the simple increased liability to death with advance in age. Dr. Ogle has studied the relation between cancer deaths and total deaths and has constructed a table showing the ratio of total deaths to one of cancer which in part is as follows:

Age periods.	Total deaths to one of cancer.
20 to 25	255
25 to 35	71
35 to 45	24
45 to 55	14
55 to 65	14
65 to 75	21
75 and upward	48

This table shows the striking reduction of the ratio of general deaths to those due to cancer from 255 to 1 between the ages of twenty and twenty-five, to 14 to 1 between the ages of forty-five to sixty-five.

A study of age incidence in cancer brings out one very interesting point that is somewhat opposed to the common belief in the matter. Namely, the very aged are relatively much less prone to the disease than their juniors, while in extreme old age cancer is very rare indeed. Williams states that of 1,087 centenarians only 5 died of cancer, or 1 in 217; of 202 other individuals ninety years of age and upward, there was not a single instance of malignant disease; in 622 persons between eighty and ninety years old there were only fourteen instances of it. In these sets of figures mortality from cancer in the females was somewhat higher than in males. Williams lays special stress on these and similar tabulations, for according to him, they show that cancer is not a disease of senility, however general may be the opposite belief. "The special feature in the age incidence of malignant disease is its connection with decline in reproductive activity and not in its fancied relation to senility."

Not only numerous cases of congenital tumors have been reported but it is probable that many cancers of early life are of prenatal origin. Such tumors, naturally, have much to do with errors of development and their localization is, therefore, quite different from most tumors of adult life; the eye, kidney, testis, prostate, and bones are the most frequently affected structures. Most of the tumors of early life are sarcomatous in nature; some of the congenital tumors are teratomata, while others are of mixed connective tissue and epithelial elements, the former usually predominating. Indeed, carcinoma is a very rare disease before puberty, the rectum being the only organ that is not infrequently affected by a tumor of this nature. Malignant disease of the stomach is very rare in childhood. Women up to the age of twenty are almost exempt from cancer of the breast; of 500 patients with cancer of the breast observed by Williams, the youngest was twenty-four years old at the time of onset. Gross had one patient twenty-one years old among 1,622 cases; Bryant observed a patient twenty and one-half years old, and Henry saw one twenty-one years old.

The facts brought out in reference to the influence of age upon the incidence of cancer are assumed to be of great importance by Williams and his comment deserves to be quoted *in extenso:* "We learn from the foregoing facts, that while the forces of growth, development and reproduction are in greatest activity —during the periods of prenatal life, infancy, childhood, adolescence, and adult age—the tendency to malignant tumors of any kind is exceedingly small. In both sexes the disease begins to be frequent as soon as the period of perfection has been attained, *i.e.* after the thirty-fifth year; during middle age and the decline of life the proclivity to it increases until about the sixty-fifth year, after which it becomes relatively less frequent, and increasingly so as age advances. The principles that govern the age incidence of malignant disease in general apply also to its various local manifestations in both sexes. That some parts of the body—such as uterus, ovary, and mamma—are attacked earlier than others, may be ascribed to the

fact that the former attain maturity earlier than the latter. Thus the liability to malignant disease waxes, as the developmental and reproductive activities wane. . . . . We have thus an illustration of the universal biological law, that growth varies according to the surplus of nutrition over expenditure. So long as the surplus exists—that is to say, while nutrition is relatively high—simple continuous growth is maintained; but when nutrition is relatively low—that is to say, when it is nearly equalled by expenditure—new centers of development are apt to arise and growth tends to become *discontinuous*."

Sex.—The influence of sex on the incidence and localization of cancer is very marked, women being more liable to the disease because of the frequency with which their reproductive organs are involved. In speaking of the influence of age upon cancer we have noted that C. P. White's charts show the greatest incidence in females at fifty and in males at fifty-five. Yet if the tumors of the breast, uterus, and ovaries are omitted, the age of greatest incidence in the females approaches that of the male, so that the curves of incidence are almost superimposed. The mere incidence of cancer, too, is much higher in the female sex, the sex ratio in mortality figures usually showing a proportion of 1 to 1.3 or 1 to 1.5. That numerous factors enter into those proportions making them only approximately correct is shown by the great differences in the statistical estimation of the incidence of cancer in the two sexes. Thus for every 100 deaths from cancer in males, there occurred in

United States	171.0 deaths in the female sex (1900).
Sweden	153.8 deaths in the female sex (1891–1895).
England	147.0 deaths in the female sex (1901–1905).
Italy	127.8 deaths in the female sex (1904).
Hungary	124.7 deaths in the female sex (1901–1904).
Germany	123.0 deaths in the female sex (1907).
Austria	121.0 deaths in the female sex (1895–1898).
Switzerland	100.2 deaths in the female sex (1901–1906).

It is noteworthy that Germany, Austria, and Switzerland, countries in which statistical studies have been most accurate, show least difference in the incidence between the two sexes. Collective investigations of living cancer patients on a certain date have likewise shown a higher incidence among the females, one reason for this being probably the ease with which cancer of the female reproductive organs may be recognized as compared with the frequent cancer of the stomach in the male. Among the general statements on this question is an interesting one of Crile's who says that in the United States one woman in eight who reaches her thirty-fifth year dies of cancer.

Heredity.—Heredity in disease has received a new aspect since the confirmation of the discoveries made by Mendel in the last century and quite unnoticed at the time. It is generally believed now that Weismann is right in claiming that acquired characteristics are not inherited. In applying this idea to cancer we should not look for inherited tendency to cancer in families in the members of which examples of the acquired type of cancer have occurred, the term acquired being applied to such instances of the disease as are clearly connected with some causal factor, such as chronic irritation. Several instances of such cancer in the same family may be explained rather by the existence of the same environment and therefore of the same causative factors than by inheritance of the tendency to malignant disease.

On the other hand, families in which cancer appears spontaneously, so far as our present knowledge of the etiological factors is concerned, are the ones whose history should be carefully studied with the view of ascertaining any unusual tendency to malignant disease. The trouble with numerous statistics having to do with heredity in cancer is that these two clearly different types have not been distinguished in taking the family history of cancer patients. Surely the fact that several progenitors of a patient suffering from a cancer of the lip having undoubted connection with the habit of smoking a clay pipe, or of a chimney-sweep suffering from cancer of the scrotum, have died of cancer of the breast or of the internal organs proves nothing whatever about the influence of heredity on cancer. On the other hand, several instances in one family of cancer of apparently spontaneous origin affecting perhaps the same organs should go far to prove that heredity in such a family plays an unmistakable rôle, because such an occurrence may be looked upon as a spontaneous variation or mutation, the inheritability of which has recently been proved by the researches of de Vries and others.

Of the numerous examples of cancer in families, only two well-known examples need be mentioned. Broca's case of Madame Z., of whose twenty-six descendants who attained or exceeded the age of thirty, fifteen died of cancer; and the cases of cancer of the stomach in the Bonaparte family, Napoleon, his father, his brother, and two of his sisters all having died of cancer of the stomach. In these instances the tendency to cancer may be looked upon as a dominant characteristic in the Mendelian sense. Such data are fair presumptive evidence of the hereditary influence in cancer, and such influence must be accepted as probable though requiring much elucidation by newer investigations.

Trauma.—History of repeated or single injury is frequently given by cancer patients but such testimony is due more to the unconscious attempt on their part to account for the appearance of the disease, their minds refusing to recognize an apparently causeless affection, than to any real relation between trauma and their cancers. On the other hand, numerous medical observers believe in the importance of trauma in cancer, and certain statistics, especially in the case of sarcoma, bear out such a relation fairly well. Thus, Coley has noted a definite history of trauma in 225 of 970 cases of sarcoma, or in twenty-three per cent. of the cases observed by him. The fact, too, that in fifty-two per cent. of these cases the tumor developed within the first month after injury makes Coley believe that "acute traumatic malignancy" is an actuality. Samuel Gross obtained a history of previous injury in nearly fifty per cent. of his (165) cases of sarcoma of the long bones. Carl Lowenthal on the basis of very abundant material thinks that the conclusion that external injury may undoubtedly give rise to the development of tumor is quite justified.

Of 250 cases of carcinoma observed by Coley 82 or 32.8 per cent., gave a history of trauma; of them, cancers of the breast had a history of a single antecedent injury in 43 per cent. of cases. McWilliams says that of the 69 patients with cancer of the breast in the Presbyterian Hospital of New York in whom records on that point were complete, 29 or 44.6 per cent. gave a history of a distinct antecedent trauma. Numerous other statistical studies confirm these statements especially with reference to the rôle of trauma in the causation of sarcoma.

On the other hand, Roger Williams denies any such relationship between cancer and trauma, maintaining that if any existed, cancers should be much more frequent among men, who suffer very much from traumata, than among women, who are more exempt, while the opposite is the actual fact. In case of the breast, too, the nipple and the areola are most exposed to injury and yet the greatest numbers of cancers of the breast have the glandular tissue for the starting-point. Moreover, the head and the extremities are more subject to injury, yet cancers of these parts are much rarer than of the trunk and of the internal organs. Williams brings out the point that cancers usually have a single starting-point, while if trauma were an effective cause, cancers with multiple points of origin should be frequent. Experimental attempts to produce cancer by inflicting single severe or re-

peated slight injuries have not been successful. He concludes that injury very frequently simply calls the attention of the patient to a cancer which has been gradually and silently developing.

So-called "acute traumatic malignancy" is supposed to exist when a very recent injury is followed by the development of cancer. Most of the published cases of this nature involve fractures with the development of sarcoma; it must be remembered that sarcoma is not an infrequent cause of "pathological" fractures of bones, so that occasionally the relation may have been the reverse from what is supposed by the assumption of acute traumatic malignancy. Moreover, malignant disease in conjunction with fractures is very rare in comparison to the great number of fractures; surely, more instances of malignancy should be encountered. Other instances of "acute traumatic malignancy," however, involve accidental and rare forms of injury and the above objections do not hold for them. Legally, the possibility of a causal relation between injury and malignant disease has been accepted in countries in which pensions and indemnities for injuries are included in government insurance schemes.

The whole question of the relation of trauma to cancer is not, then, settled and there are ardent advocates on both sides. Wolff concludes a survey of the literature on the influence of trauma upon the appearance of cancer with the following statements: "Acute trauma can never change normal cells into cancer cells and lead to malignant overgrowth of the same . . . . . The possibility exists, however, that acute trauma may act as the exciting factor in the development of cancer, if it has affected pathologically changed cells, or embryonal cells, or organs, or cells that have assumed embryonal characteristics later in life . . . . . On the other hand, clinical experience teaches us that a latent cancer may become manifest after injury or an already evident cancer may, after an injury, run a more malignant and rapid course."

Chronic Injuries.—A more important etiological factor in the causation of cancer is to be found in the effects of small but constantly repeated injuries either of physical or chemical nature. A most interesting instance of this relation is shown in the so-called *kangri* cancer in Kashmir. Neve states in a recent communication that of the 1770 malignant tumors removed at the Kashmir Mission Hospital in the last twenty-five years 1189 were epitheliomata and of the latter 848 were located on the thighs or abdomen, because of the irritation caused by the *kangri*, a portable fire basket carried by the people under their clothes. When the native is sitting down, this basket rests against the insides of the thighs or the front of the abdomen. Other portions on the anterior surface of the body exposed to the action of heat occasionally developed cancer but the proportion of these cases was small. Scars from burns were frequent starting-points of the epitheliomata.

The relation between chronic ulcers of the stomach and cancer of that organ will be discussed in the special article on diseases of the stomach, but it may be stated here that recent examinations of ulcers removed at operation showed a much higher percentage of malignant degeneration that was thought probable a few years ago. Of course, chronic irritation by the passage of food and chemical irritation by the gastric juice and the food are the possible etiological factors in this instance as well as the chronicity itself of such ulcers.

Chemical Irritants.—Clinical observations have long ago shown that certain substances with which workers in different trades come in contact in the course of the work hold a certain causal relation to the development of cancer.

Soot.—Percival Pott noted as long ago as 1775 that chimney sweeps are frequently affected by a disease of the scrotum which he recognized as cancerous in nature. Later observers showed that the scrotum was not the exclusive site of the affection but that other parts that come into constant contact with soot are apt to be attacked, *e.g.* the back of the hand. The rôle of soot is shown by the great diminution of this "chimney sweep's cancer" since the introduction of different construction of chimneys and different ways of cleaning them of accumulated soot.

Workers in *tar or paraffin* are frequently affected by chronic skin diseases which in many instances undergo malignant degeneration. Thus, five out of twenty tar workers recently examined by Schamberg showed evidence of beginning or well-developed cancer.

The irritating properties of *tobacco juice* and *smoke* have been blamed for the frequency of cancers of the lip and mouth. That tobacco alone cannot explain all such cases is seen from the occurrence of cases among non-smokers and the fact that cancers of the lip, tongue, and mucous membranes of the mouth were known long before tobacco came into general use. It is quite probable that the chronic injury caused by *bad teeth* may play a rôle in some of the cancers of the mouth. The heat transmitted by the pipe stem as well as the slight trauma caused by the rough clay of the pipe may add to the injurious effects of the purely chemical irritants in tobacco.

Of late, experimental evidence of the probable action of chemical irritants has been brought forward by the demonstration that certain chemicals, especially aromatic amido derivatives, are capable of stimulating the growth of epithelium sufficiently to enable it to invade the subjacent connective tissues. Hutchinson long ago made the observation that arsenic taken internally seems to have the power of predisposing toward cancers of the skin especially on the hands and soles of the feet. Writing as late as April, 1911, he repeats that his observations have been fully corroborated with time and states that he considers the use of the drug dangerous unless the clearest indication exists for its employment. The newer arsenic derivatives atoxyl, salvarsan, etc., have not been used for a sufficiently long time to show whether they share this alleged dangerous property with the older forms of arsenical medication.

Physical Agents.—It has long ago been observed that constant exposure to *wind* and *weather* and especially to *sunlight* seems to favor the development of cancerous affections of the skin. Thus Thiersch pointed out the frequency of facial cancers in peasants. Sailors have been shown to be subject to a disease of the skin, xeroderma pigmentosum, which is marked by atrophy of the skin with increase of pigment; in a number of individuals this affection goes on until it reaches a chronic eczematous character which may then assume malignant properties. Because of the numerous examples of this primary affection in several members of the same family it may be assumed that there exists some internal factor favoring its development, while the malignant nature may be superimposed on that because of the effects of constant exposure to sunlight.

Of wider interest is the rôle of x-rays in the causation of cancer. Short exposure to the rays may leave no obvious effects on the skin; longer exposures result in epilation temporary or permanent, erythema, vesication, ulceration, and finally gangrene, depending upon the duration and the degree of application. Incurable dermatitis follows repeated exposures for short periods such as were frequent in the case of the early workers with the rays, before they recognized the dangers attendant upon their use. Indolent and intractable ulceration frequently follows in the wake of this dermatitis and the final result may be malignant degeneration of the tissue with the development of epitheliomata. Several of the pioneer workers in the field have lost their lives from the consequences of this affection and a number have had to suffer amputations of their hands or arms.

Ulcers, Scars, and Fistulæ.—Chronic ulcerative processes seem to afford favorable ground for the development of cancer. Usually an ulcer of long duration, the healing of which is prevented by some constitutional cause or a local condition, continues to show abundant granulation tissue which serves as an irritative moment to the surrounding epithelium. Gradually the epithelial edges show much proliferation of tissue, as evidenced by induration and finally a slowly growing epithelioma results. Occasionally, a chronic fistula depending upon simple suppurative or tuberculous osteomyelitis shows similar change, its edges undergoing malignant degeneration. The constant irritation of the discharge may here be looked upon as the traumatic influence favoring the appearance of cancer. Scars sometimes behave in the same fashion: simple increase in the scar elements leads to hypertrophy of the resulting structure and the formation of a keloid, while multiplication of the epithelium and its invasion of the granulating or scar tissue and the neighboring structures leads to the appearance of an epithelioma. Scars of burns are most apt to undergo the latter kind of transformation. Occasionally, operative scars develop into malignant tissue, cases having been published showing the involvement of laparotomy scars, of scars of operation for hernia, of amputation stumps and scars following operation on bones.

Nævi.—It has long been recognized that nævi are prone to undergo malignant degeneration and the advent of Cohnheim's hypothesis of the relation of embryonal rests to cancer further strengthened the conclusions derived from clinical observations. Mechanical injury of long duration seems again to be the actual factor exciting the transformation of these benign structures into malignant tumors. Ribbert thinks that nævi possess certain cells which are concerned with the elaboration of pigment and it is these cells that are probably responsible for the malignant change in the structures. Tumors developing from pigmented moles are usually extremely malignant because they very readily lead to the formation of metastases in various parts of the body. These metastases are pigmented just as the original tumors.

Precancerous States.—*Leucoplakia.*—Numerous affections have been so often observed to precede the development of cancer that a certain causal relationship between them has been established. These conditions are usually termed *precancerous*. Perhaps the most important one is leucoplakia, or hyperplastic change in the surface epithelium, most frequently and typically observed in the mucous membrane of the tongue and mouth. The chief etiological factors in the development of this affection seem to be syphilis and the use of tobacco. Numerous cases, however, have no such etiology. Fournier has investigated 321 cases of this affection and has found that 97 or 30 per cent. have eventually ended in cancer. Of 219 cases of lingual and buccal cancers, tabulated by Williams, 47 or about 22 per cent. showed preexisting lesions of leucoplakia. The latter, however, is a chronic affection and its cancerous degeneration does not usually take place until the age period fifty to sixty is reached.

Paget's Disease of the Nipple.—This is a chronic affection of the nipple and the neighboring skin which is said finally to change into epithelioma. Most observers, however, claim that the disease is cancerous from the start and resembles eczema in appearance only. Its appearance in elderly women, the induration of the edges, and persistence in spite of the usual therapy are quoted to prove its cancerous nature. In any case, it has nothing to do with the causation of the usual type of breast cancer.

Lupus.—We have seen that chronic ulcers, scars of accidental injury and of operations, fistulæ, etc., frequently become sites of cancers. Occasionally, a specific affection of chronic nature may prepare the soil for the appearance of cancer. This is most often the case with lupus of tuberculous nature, and the usual explanation is found in the constant irritation of the skin produced by the disease itself, aided, perhaps, by the various therapeutic measures adopted. Usually cancer develops in the scars left by the preceding lupus, but occasionally it starts from the active nodule itself. Sequeira states that epithelioma develops in about two per cent. of old cases of lupus; it rarely occurs unless the disease has been in progress for twenty years. He thinks that prolonged treatment with *x*-rays especially tends to produce malignant change in lupus.

Other Diseases and Cancer.—*Tuberculosis.*—Some attention has been given to the relation of cancer to other diseases and of these tuberculosis, syphilis, and erysipelas deserve discussion. In the beginning of this century some of the foremost medical observers denied the possibility of coexistence of cancer and tuberculosis, because of the alleged refractory behavior of the body affected by one specific disease toward any other affection. Hunter in England and Rokitansky in Vienna were the chief defenders of this theory; when, however, cases of coincident tuberculosis and cancer became to be frequently reported, the latter modified his views slightly, claiming that tuberculosis appeared only when cancer has reached the ulcerative and necrotic state, and *vice versa*, the body being then free of one or the other specific "dyscrasia." These views have proved to be untenable, for cancer has been observed in all stages of tuberculosis, and indeed, even to develop occasionally on the basis of a tuberculous lesion; a combination of cancer and tuberculosis is said by several modern observers to occur in from nine to twenty per cent. of cases of cancer.

Roger Williams thinks that there is a close relation between cancer and tubercle. According to him, a large proportion of cancerous patients are the surviving members of tuberculous families, and those who survive the peculiar kind of degeneracy associated with the tuberculous predisposition, are at a later period of life especially prone to cancer. On the other hand, he grants that a certain antagonism exists between active tuberculous and cancerous manifestations, the special causative factors which favor the one being inimical to the other.

These views are interesting but it must be remembered that "tuberculous predisposition" is a very indefinite factor. Because of the great prevalence of tuberculosis in the community, it is very difficult to state which families are subject to such predisposition, and which show simply accidental cases of tuberculosis. Moreover, as Moak has pointed out, tuberculosis and cancer show a great difference in age incidence, most cases of tuberculosis being fatal before fifty, and most cases of cancer after fifty. On the whole, the few data may be used in support of either interpretation of the relation between cancer and tubercle, and this has been the case, to judge from the literature. It may be doubted whether any definite conclusions are possible with our present ignorance of cancer etiology; experimental work with animal neoplasms and their transmissibility to tuberculous individuals should throw some light on the subject.

Many authors defend the thesis that tuberculous inflammation may act as a local predisposing factor toward the development of cancer. Lubarsch thinks that it may act simply as a chronic and continuous trauma; Ribbert points out the stimulation of tissue and especially of epithelium caused by tuberculosis; Wolff thinks that scar formation commonly seen in very chronic tuberculosis, may act as the predisposing moment. The frequency of cancerous degeneration of lupus scars has already been mentioned.

Syphilis.—The older observers of cancer have fre-

quently thought that syphilis has some causal relation to cancer. Esmarch among them has pointed out that syphilis favors overgrowth of connective tissue and thus predisposes to the connective-tissue type of malignant disease, that is, sarcoma. Many cases of carcinomatous degeneration of late syphilitic lesions have been reported; these, of course, may be interpreted as showing simple local predisposition to cancer common to all scar-forming diseases.

On the other hand, a few writers claim that there exists a marked antithesis between cancer and syphilis. Both these diseases are common in the community and coincident appearance of them should be rather frequent. Williams, however, states that of 165 consecutive female breast-cancer patients not a single one presented undoubted signs of having had syphilis; and of 160 uterine cancer patients only one presented signs of having had syphilis. Williams thinks, in accordance with his general conception of cancer etiology, that the probable immunity of syphilitics is due to the depraved nutrition and lowered vitality of the subjects of this disease. It must, of course, be remembered that within the last decade it has been shown that syphilis in the female may run a completely hidden course and not leave its "signature," as Ricord termed it. There has been no extensive examination of cancer patients with the help of the Wassermann reaction from this point of view, and such a one would be very desirable. The percentage of syphilitic patients in the hospitals is fairly accurately estimated by means of this reaction and this compared with like results in cancer patients would throw light upon the alleged immunity of syphilitic patients.

Erysipelas.—It has always been the tradition that occasionally an attack of erysipelas in the course of a cancer may lead to a temporary or even permanent disappearance of the tumor. This is especially the case with tumors of sarcomatous nature. Busch reported three such cases as far back as 1866, and Bruns in 1888 was able to collect sixteen cases of same nature; five of these were sarcomata and three of them disappeared permanently after a sharp attack of erysipelas. Carcinomata, on the other hand, while disappearing for a time always recurred sooner or later. Bruns thought that inoculation with erysipelas for therapeutic purposes is justifiable in cases of inoperable cancer.

Recently, Rovsing confirmed the above observations, having himself seen the disappearance of inoperable sarcomata after an attack of erysipelas in two instances. One patient, who was thus cured of a large recurrent osteosarcoma of the scapula with infiltration of the surrounding muscles was found to be well seventeen years later. Rovsing has also seen an epithelioma of the lip disappear after an erysipelas; and has observed temporary recession of carcinomatous tumors in other instances. He says that artificial inoculation with erysipelas has been attempted but has been given up, first, because it did not take very readily and, secondly, because it proved to be fatal to several patients as its severity, of course, could not be controlled. Other observers do not consider that erysipelas exercises any specific influence upon malignant disease, the modifying element being the fever accompanying the disease. Williams draws upon his large experience in the Middlesex Hospital where he has often seen cancer patients attacked with erysipelas but has never noticed any consequent marked amelioration of symptoms, much less anything approaching a cure. He thinks that diagnostic mistakes are the probable explanation of the fairly numerous reported cases in which erysipelas is alleged to have proved salutary in cancer. Mere arrest or regression of the tumor he attributes not to any specific agency of the toxins of erysipelas but to the not unusual effect of an intercurrent disease, especially one accompanied by fever and leading to marked enfeeblement of the patient.

W. B. Coley has collected thirty-eight cases of erysipelas occurring in the course of malignant disease, accidentally in twenty-three, inoculated in fifteen. Seventeen of these were cases of sarcoma, seventeen carcinoma, and four not positively diagnosed. Of the carcinomata, three cases are alleged to have been permanently cured and thirteen were temporarily improved. Of the seventeen sarcoma cases, seven or forty-one per cent. were well, that is, had no recurrence, from one to seven years after the attack. Ten showed improvement, the tumor having disappeared to be followed by a recurrence. Coley concludes that inoculation with erysipelas is very difficult and its effects cannot be controlled. This has led him to use the toxins of the streptococcus derived from cases of erysipelas, first alone and then in combination with the toxins of *Bacillus prodigiosus* in the treatment of sarcoma. (See under Treatment.)

General Clinical Phenomena.—The physical characteristics of cancer that are open to determination by clinical methods are so varied, because of the differences in the anatomical type of tumors, in their age and their localization in the organism that only a few points can be mentioned in a discussion of cancer in general. Such characteristics as can be elicited by the usual clinical methods of inspection, palpation and occasionally auscultation, will be discussed in the special articles on diseases of the various organs of the body. However, there are a few traits common to cancer in general and some of them will find mention in this section.

Cancers may be circumscribed or diffuse. Among malignant growths sarcomata are more frequently circumscribed than carcinomata. Such tumors may be round or oval, may have smooth surfaces or be nodular, may be uniform to palpation or consist of several masses joined together. If the surface of the tumor shows numerous projections with fairly small bases, a papillary structure results. If the bases of the projections are fairly wide and they are of considerable size, a "cauliflower" growth results. The word polyp is used to describe tumors that are connected with the mother tumor or other tissues by a long pedicle. Such polyps may be single or multiple. The word is usually applied to smaller tumor masses, the larger being simply called pedunculated growths. Carcinomata usually show a diffuse growth, because of the much greater tendency to infiltrate surrounding tissues than is seen in sarcomata. The latter may even show a pseudocapsule, thus simulating benign tumors.

In *size*, cancers differ very widely, although sarcomata usually appear larger because of their circumscribed mode of growth. Carcinomata occasionally shrink so much because of connective tissue in them that a part affected may be smaller than the normal organ, as instanced very frequently in scirrhus cancers of the breast. Very large tumors are more frequently non-malignant than malignant, if externally situated; internal cancers may reach very large size.

Cancers vary almost as much in *consistency* as in size, the amount of fibrous tissue, the type of tumor, the rate of growth, the presence of necrosis being the various modifying elements. Deep-seated tumors usually feel hard as any fairly circumscribed tissue feels under the soft overlying parts. The skin over sarcomata may be unchanged or slightly inflamed. It may be tense and very thin so as to show the large underlying veins. It may be attached to the tumor in its later stages. The capillaries of the skin are frequently injected and the neighboring veins usually dilated. Occasionally the tumor breaks through the skin and forms a rapidly growing projecting mass. This occurrence is usually followed by extensive ulceration and infection of the tumor which ends in necrosis and hemorrhage. The course of sarcomata is varied; some are very rapidly growing and result

fatally in a few months after the onset of the disease (tonsillar tumors, lymph-node tumors). Tumors originating in the fasciæ, periosteum, and bones are usually slower in growth. Sarcomata form metastases early but usually not in neighboring lymph nodes. They spread through the blood-vessels, masses of cells entering the thin-walled vessels and being carried as emboli.

Carcinomata are usually more intimately connected with surrounding structures than sarcomata, because of the greater proclivity to infiltrating growth. They are therefore little movable on the underlying structures, and the skin becomes early attached to the surface of the tumor. The skin is usually changed in color, being reddish brown, very frequently quite thin, and ulcerated. Carcinomatous ulcers are characterized by having hard, stiff, overhanging edges. The bases of the ulcers are likewise firm, uneven, and covered by serosanguineous fluid or thin pus. Usually a few local extensions may be felt through the surrounding skin, some of them attached to the original tumor by strands of cancer tissue, others apparently free, the results of "disconnected growth." The regional lymph nodes are early involved, though they may be enlarged only because of simple inflammation. They quickly enlarge, become fixed to surrounding structures, and may rapidly overshadow in size the original tumor.

We have named in our discussion of the definition of cancer the several clinical features that may be looked upon as characteristics of malignancy but of these *persistence* is really a feature of all tumors, malignant and benign. More characteristic is *infiltration* of surrounding structures, which is almost universal in epithelial tumors but not so common in sarcomata. Yet some kind of infiltration takes place in certain inflammatory lesions and still more strikingly in the growth of the trophoblast and the development of the placenta; the latter process sometimes actually goes on to an extent which results in the formation of a malignant tumor, deciduoma malignum, a tumor, the study of which is still recent and may throw much light upon the growth of tumors in general.

Dissemination is another property which is partly shared with tumors by the trophoblast. Clinically it is of the greatest importance. Such dissemination takes place by the transportation of tumor cells through lymph channels and leads to the spread of malignant disease through the regional lymph nodes. Because of the many badly formed blood spaces or vessels in the tumor its substance often breaks through them and cancer cells are then carried into the general circulation, leading to distant metastases or to general dissemination of the disease. Clinically, the three stages, that is, the primary tumor, the appearance of regional lymph-node infection, and thirdly, general dissemination of the disease, are important: the first is most favorable for complete cure by surgical operation; the second necessitates wide excision of the original tumor and the removal of all regional lymph nodes, recurrences being frequent; the third stage is hopeless, for the tumor has reached the inoperable stage, the whole organism being involved.

It is probable that cancer cells reach the lymph or blood circulation early in the life of the tumor, but the earlier emboli are destroyed by the tissue. Perhaps the growth of the tumor itself prepares the body for the dissemination of cancer, robbing it of some fine protective mechanism.

Frequently metastatic tumors grow more rapidly than the original tumor, and this fact should not be lost sight of in looking for the organ affected by the primary growth. According to Tillmanns, metastases are most frequent in the lymph nodes, liver, lung, pleura, peritoneum, kidney, bones, and spleen, in the order named, though of course the earliest structure involved usually depends upon the site of the original growth.

Another form of dissemination of tumors is seen in serous surfaces, where small parts detached from ulcerated parts of intraabdominal tumors are simply grafted on the peritoneal surface. A few of the favorite sites of metastases should be mentioned, being important from the standpoint of diagnosis. Metastases in the bones may lead to spontaneous fractures; if the vertebræ are involved the signs may simulate tuberculous disease of the spine. Occasionally, if the marrow is involved, myelocytes appear in the blood in moderate numbers. This occurrence, in the presence of an anemia, may be fairly diagnostic in obscure cases. Breast cancers, cancers of the prostate, and cancers of the thyroid gland are most apt to result in metastases of the bones. The heart and blood-vessels are very seldom affected by primary cancers but are not infrequently seats of secondary growths. Strangely enough such involvement of the heart rarely produces very marked clinical symptoms. Rarely, a malignant nodule may be situated so that conduction is interfered with and some type of arrhythmia results. The valves are almost never affected by secondary growths.

Recurrence.—By recurrence is meant the reappearance of malignant disease in the locality occupied by the primary tumor, in the immediate neighborhood, in the regional lymph nodes, or in the distant parts of the body, after operative or other interference that has apparently insured the destruction of the disease. Local recurrences are best observed in mammary cancer where they present themselves as small nodules in the scar or in its immediate neighborhood from a few weeks to several years after operation. The incidence of such recurrence is very much influenced by the stage of cancer at the time of operation, advanced cancer being, of course, more liable to recur, and especially by the nature of the operation, recent thorough methods of removal having very much diminished the probability of recurrence. This fact tends to confirm the usual explanation of recurrence by the assumption that a few cancer cells are left at the extirpation and "take root" in the same favorable soil that resulted in the primary disease. The latter had one starting point; at this time, however, the disease possesses many new centers which serve as multiple foci for further spread of the tumor. Some of the foci may be explained by the assumption of inoculation during operation, as for example the frequently seen nodules in the stitch wounds or in the operative scar.

Recurrence usually takes place early after the operation. Williams has calculated that sixty-four per cent. of all mammary cancer recurrences take place within the first six months after operation, and about two-thirds of these appear within the first three months. The new cancer centers may be followed by second or even third recurrences after operative removal; occasionally even more numerous recurrences have been observed, though usually the disease is either destroyed by the repeated operations or the patient succumbs to involvement of distant parts of the body.

Recurrence in the lymph nodes or in the distant organs must be explained by the assumption that dissemination of the disease has taken place even before the operation. Examples of very late recurrence, many years after the operation, have forced the assumption of a possible latency of cancer cells; thus, a pigmented cancer of the liver appearing many years after the extirpation of the primary disease affecting one eye is best explained by such an hypothesis. Late local recurrence, on the other hand, may be interpreted as a result of continuation of the same conditions as have led to the appearance of the primary malignant disease.

Changes in the Blood.—The blood in cancer shows changes characteristic of a secondary anemia. The red corpuscles are usually moderately or markedly diminished, depending upon the stage of the disease,

though such diminution very rarely reaches the very low figures common in primary pernicious anemia. Nucleated red blood cells are fairly common in advanced stages of the disease; they are usually of the normoblastic variety, megaloblasts being very rarely met with. Small red cells (microcytes) as well as irregularly shaped cells (poikilocytes) are fairly frequent. Blood platelets are apparently either normal in numbers or increased.

The hemoglobin is markedly diminished, even out of proportion to the diminution of the red blood cells. Leucocytes are usually moderately increased, polynuclear cells showing a relative as well as an absolute increase. An important feature is the absence of the usual physiological "digestive leucocytosis" in a great many cases of cancer; this feature is so frequent as to be of some diagnostic importance. Myelocytes are more frequent in cancer than in any other disease except the primary affections of the blood. They may reach very high percentages with the occurrence of metastatic growths in the bones so that the blood picture may resemble very closely that of a myeloid leukemia.

The most marked anemia occurs with cancer of the stomach and the blood picture may appear very much like that of a primary pernicious anemia. There are several points of difference, however, one being the low color index in cancer anemia, another the usual increase in leucocytes, with relative or even absolute increase in the polynuclear forms. In pernicious anemia the leucocytes are either normal or diminished in number, while the lymphocytes may show a slight relative or absolute increase.

In general the grade of anemia in cancer depends upon the site of the tumor, the stage of the disease, the rate of its growth, and also upon the character of the tumor. A tumor which presses upon or infiltrates important structures will lead to anemia quicker than cancers elsewhere; thus, tumors of the gastrointestinal tract are accompanied by most marked changes in the blood. A slowly growing cancer of the breast may result in but little change in the blood, while a rapidly growing small-celled sarcoma may lead quickly to a very marked anemia.

The anemia of cancer is due to the mechanical interference with the physiological processes of the body; to the absorption of the products of necrosis and infection which frequently takes place in tumor tissue; and perhaps to some specific products of the metabolism of cancer cells, which may have a direct destructive effect upon the blood. Numerous substances of such nature have been described but it can hardly be said that their relation to the anemia of cancer has been proved beyond reasonable doubt.

Changes in the Urine.—No specific changes in the urine accompany the appearance and growth of cancer in the body. At one time the diminution in excretion of urea was looked upon as fairly significant, but such diminution depends more upon the modified diet taken by cancer patients in the advanced stages of the disease than upon any effect of the disease itself. Forced feeding with nitrogenous food stuffs usually leads to increase in excretion of urea. Progressive "demineralization," much the same as has been noted by the French writers in tuberculosis, has likewise been observed in cancer. The diminution of chlorides in this connection may simply be a sign of involvement of the kidneys or a change in the diet of the patient and not anything characteristic of cancer. Some workers have pointed out that the urine of cancer patients is much more toxic for animals than normal urine; the standards of toxicity of the urine and the means of measuring it, however, are not at all accepted generally.

Of more interest is the authenticated observation that so-called "colloidal" nitrogen, or nitrogen precipitated by alcohol, is increased in cancer. This type of urine nitrogen is apparently increased in all affections in which much colloidal substance passes into the lymph or blood; this occurs with cancer, but likewise with cirrhosis of the liver, pleurisy with effusion, suppurative processes, etc. The determination of colloidal nitrogen may, however, be of some diagnostic importance; a negative finding may be of special value in obscure cases of disease.

Cancerous Cachexia.—The sum total of the effects of cancer upon the animal organism, consisting of pallor, emaciation, loss of appetite, and ending in marked asthenia is included under the term cachexia. This condition is most frequent with cancer, yet it is not at all a specific manifestation of this disease. Numerous other illnesses produce a state which in general resembles cachexia, as for example, constant repeated hemorrhages, chronic suppurative processes, etc. Yet the condition is of general clinical importance because it is associated with cancer more frequently than with any other affection. There are two views held in explanation of it, one supposing that the tumor *per se* is responsible for the impaired nutrition of the organism, another tracing it to the appearance of degenerative changes in the tumor with the consequences of absorption of the resulting septic or necrotic material.

The cachectic symptoms do not precede cancer as had been supposed at one time, when the cancer diathesis or dyscrasia was supposed to be an actual condition. It often disappears with removal of the tumor and may recur with the appearance and growth of metastases; it need not be accompanied by fever or any other signs of septic absorption. It is accordingly dependent upon the local disease itself and not upon any general condition of the body predisposing to cancer or developing with its growth. Numerous other authors consider it due to a special cancer toxin which they interpret as a product of the metabolism of cancer cells. The more acceptable view, however, traces the appearance of cachexia to the proneness with which cancer cells undergo degeneration. On the other hand, cachexia is most manifest in cancers of the gastrointestinal tract and here the explanation lies in the more marked absorption of toxic material from the degenerated tissue and also the interference with the functions of digestion. Such rapid cachexia is especially to be contrasted with the frequently very moderate changes in the general health coincident with a large tumor of the breast; as soon, however, as internal metastases appear and, in addition to their liability to degeneration, attack digestive organs, cachexia very quickly develops.

Clinically, cancer cachexia is marked by pallor, the skin being waxy in appearance with a peculiar lemon tint. While striking in appearance, such pallor is met with in primary pernicious anemia, in cirrhosis of the liver, and in other states accompanied by severe anemia. Emaciation is most marked in cancers of the esophagus and of the stomach, where starvation has as much to do with it as the effects of absorption of toxic substances. Indeed, many women with cancers of the breast show little emaciation to the last and while they appear waxy and pale they retain the "panniculus adiposus" very well. Loss of appetite, "dyspepsia," general muscular weakness, are other clinical evidences of cachexia.

Contagiousness of Cancer.—Everyday clinical observation speaks against contagiousness of cancer and therefore throws doubt on the authenticity of the few cases in which cancers are alleged to have been transferred from one individual to another. In the existence of so many possibilities of direct contagion as is afforded by the intimate contact with cancer patients entered into by the relatives, nurses, and doctors, certainly numerous instances of such transfer should have been observed. Williams appeals to his experience at the Middlesex Hospital during which he has never noticed anything that could be possibly construed as evidence of the communicability of

malignant disease. The wards were crowded, patients not suffering from cancer were occasionally inadvertently admitted, yet "in a period extending over twenty years not a single instance is known in which a nursing sister, probationer, nurse, ward servant, surgeon, or any one engaged in attendance on the cancer patients, ever acquired the disease." Several experimental attempts made by surgeons to inoculate themselves have been unsuccessful, the most recent of these being those of Nicholas Senn and of Wickham. Pregnancy associated with uterine cancer is not very rare, yet authentic cases of cancer of the penis acquired by sexual intercourse have not been discovered; of one hundred and eighty husbands who had marital relations with their wives who were subjects of uterine cancer, not a single one had acquired the disease (Bossi). Behla, however, defends the possibility of contagion; "*cancer à-deux*" or cancer in two persons that live in close relation with each other is fairly common, according to him. He has collected nineteen cases of carcinoma of the penis in men whose wives were subjects of uterine cancer.

Of late the contagiousness of cancer has again become the object of attention, as the recent studies of disease seemed to show that certain districts, villages, or even houses, show more extensive prevalence of cancer than the immediate neighborhood. Believers in the parasitic etiology of cancers have been especially inclined to attach much significance to such observations, correctness of which cannot be always imputed. However, in our ignorance of cancer etiology as a whole, mere prevalence of the disease in any district cannot be given much weight in proving its infectious nature. It may be that some etiological factors of which we are quite ignorant are at work in such districts, whether it be nutrition, occupation, other diseases, or any other causative factor.

In order not to make it appear that contagiousness is completely excluded by the available data it may be worth while to communicate several observations supporting such possibility. White has recently reported five cancer cases, four of them fatal, in patients who were all blood relatives or lived in close contact with one another (husband and wife); all had been infected within five years. Rovsing is inclined to accept direct contagion as a possibility. In his own family a seventy-year-old uncle died of an ulcerating osteosarcoma. His young daughter who attended him, developed universal sarcomatosis and died in two years. Rovsing thinks that cancer houses are an actuality; in one house several physicians in turn developed sarcoma and died in the course of a year or two.

Numerous attempts have been made to inoculate lower animals with cancers from human individuals and success has been claimed in a few instances. There is no doubt, however, that the vast majority of such inoculations ended in failures and the few reported successes are not beyond criticism. Higher monkeys were used by Metchnikoff and Grünbaum in several attempts to transfer human cancer, all of them ending in failure. Since animal cancers have become the subject of much research only a few instances suggesting contagion have been adduced. Uniform environment, inbreeding, constant irritation or trauma (tumors of the breast in female mice used for breeding) may well explain such isolated instances.

Diagnosis.—Such diagnostic points as are involved in the recognition of cancer of special regions are discussed in this Handbook under the diseases of the various organs. It has always been the endeavor, however, to find some means of recognizing the existence of cancer in the body without reference to its location or to any special symptoms due to involvement of the individual organs. Especially during the last decade many systematic efforts have been made to arrive at the diagnosis of cancer *per se*. It must be acknowledged that none of the signs thus found has proved pathognomonic; many, however, have a corroborative value and several are still on trial.

Precipitins.—Specific precipitins in the serum of cancer patients have been sought for by many workers. Animals were prepared by injecting them with serum of cancer patients with the hope that the serum of such animals would show specific precipitation with the serum of cancer patients. While this was occasionally the case, no uniform results of value have been obtained. Kelling, who believes that cancer is due to the development in the body of embryo cells of other species of animals, whose tissues are taken as food, has attempted to obtain precipitins with the extracts of such tissue. He claims to have obtained positive results in sufficient numbers to support his theory, especially with extracts of eggs and chicken meat. Kelling's hypothesis has received no verification elsewhere.

Maragliano, Stumm, Weil and Braun, and others, have experimented with the precipitin formation in the diagnosis of cancer. It may be stated that up to the present time no diagnostic significance can be attached to the results obtained by the use of precipitin reaction.

Meiostagmin Reaction.—This name has been applied by Ascoli to the lowering of surface tension which occurs in a mixture of specific antigen and a corresponding serum, after a two-hour inoculation in a thermostat. Roughly, the procedure consists of extracting some specific organism or diseased tissue and then adding to it the serum of the patient to be tested. The tension is tested by estimating the number of drops in a certain amount of the mixture before and after incubation, the stalagmometer of Traube being used for the purpose. If a lowering of the tension has occurred the number of drops in the same amount of fluid will be increased after inoculation. Ascoli claims that this will almost always occur with a serum containing specific antibodies for the antigen used; with Izar he has obtained positive results in syphilis, tuberculosis, typhoid fever, echinococcus disease, and lately with cancer.

Ascoli obtained positive results in fifty-eight out of sixty-two cases of malignant diseases using antigen made from rat sarcoma. Encouraging results were obtained by d'Este who saw increase in the number of drops in twelve cases of cancer while eight non-malignant tumors gave a negative reaction, and by Micheli and Cattoretti who likewise obtained almost uniformly positive results in cancer. Later reports have not been as encouraging: Kelling obtained positive results in only forty-seven per cent. of his cases, while Stuber of Bier's clinic in Berlin could get no trustworthy results whatever. Ascoli and his coworkers have in a way acknowledged that their first reports were too rosy, for they have introduced several radical changes in the technique as first described.

The reaction has been tested in the wards of the Mount Sinai Hospital, New York City, by Bernstein and Simons, and they report unfavorably upon it, having never obtained what they would consider a positive result. The test, however, is still in its infancy and the very favorable results obtained by some European workers show that it may be of value. A final judgment cannot be passed upon it at this time.

Leucodiagnosis.—This is a term applied by Achard and coworkers to a method of diagnosing various conditions by the examination of the leucocytes. These authors claim, that the presence of certain cellular elements in the organism confers upon the leucocytes the property of reacting to the products of such elements. They think that the reaction is in every case specific for such cellular substances, whether they be physiological or pathological products. The test is made with an extract of cancer

tissue. Leucocytes of normal persons seem to lose their phagocytic properties when mixed with such extracts, while leucocytes from persons suffering from cancer are not affected by the extract. The phagocytic properties are tested by the use of an emulsion of yeast to which is added a little of the extract of malignant tissue and a drop of blood from the patient. The authors report that of forty-nine cases of cancer all gave a positive reaction while of twenty-four normal persons all were negative to the test.

Hemolytic Tests for Cancer.—Weil writes that several years ago Lang showed that in advanced cases of cancer the red blood cells show a marked resistance to the lytic power of anisotonic salt solution. It was later found that a severe anemia with the presence of nucleated red cells could be produced in animals experimentally by the injections of well-known chemical substances (*e.g.* saponin) that act as hemolysins. The red blood cells of such animals showed marked resistance to hemolysis as compared with normal cells. Such an anemia resembles cancer anemia very much and because of the increased resistance of the red cells in the animals used for experiments outlined above and in human cancer cases, it seemed fair to assume that such resistance is in both cases due to a similar cause, namely, to the presence of an hemolysin in the blood. This seemed even more reasonable when it is remembered that cancer tissue has been shown to possess hemolyzing properties and the serum of cancer patients likewise may show increased hemolyzing power. Weil in this country showed that serum of dogs with experimental lymphosarcoma was markedly hemolytic for the red blood cells of normal dogs but not for the red blood cells of other tumor-bearing dogs. The reaction was so constant that it seemed possible to diagnose cancer from examination of the serum for hemolytic properties. Crile adopted the method for human cases and his first reports were very favorable. Weil, however, states that twenty-six per cent. of non-cancer patients examined by him gave the type of the reaction which was typical for tumor-bearing dogs, while only fifty-six per cent. of proved cancer cases gave a similar reaction. Of course this excluded the reaction from any pathognomonic significance, though it may have some corroborative value. Scientifically the reaction is of great interest and our knowledge of it is not at all complete.

The presence of isolysins has been shown in forty-two per cent. of the cases (714) examined by various authors, but there are great discrepancies in individual results. This may be due to the differences of technique and to various degrees of hemolysis taken as a positive reaction. Usually hemolysins are present when the tumor is well developed and when metastases are present, and they frequently disappear after a surgical removal of the tumor. They must be very rare in serum from patients with non-malignant tumors, Krieda having found that in seventy-nine published observations none showed their presence. On the other hand, other affections not infrequently lead to their appearance and this, of course, vitiates their diagnostic value; they are especially often met with in tuberculosis, though in that disease "reverse hemolysis" (Crile) occurs frequently enough to be fairly typical. In this type of the reaction the serum of the patient dissolves the red corpuscles of another individual, but in addition his red cells are dissolved by the serum of healthy individuals. Only in advanced cases of cancer was this reaction fairly frequent and in such cases confusion with tuberculosis is not very probable.

The most disquieting thing about the reaction is its frequency in normal individuals, which is much higher than was at first supposed. It was found in 19 cases out of 567 examined by several authors; that is, in 3.5 per cent. It is probable that this percentage would be higher if the blood cells of many individuals were tested against the serum examined.

Cutaneous Hemolytic Test.—Elsberg and coworkers have found that subcutaneous injections of human blood cells are in certain individuals followed by a very characteristic skin reaction. In applying the test to patients they discovered that 89.9 per cent. of those that responded with a positive reaction were suffering from carcinoma, while 94.3 per cent. of those that gave no reaction were free from cancer.

This reaction has been tried by several other observers and quite conflicting reports have appeared in the literature. Of course, it is simply a modification of the general hemolytic reaction but the use of the subcutaneous method makes it easier to carry out and may perhaps add to its delicacy. Risley tried it in 73 non-malignant cases and it proved positive in 15, negative in 55, and doubtful in three of them. Of 27 cases of cancer 9 gave a positive reaction, 16 were negative, while 2 were doubtful. Risley concludes that the test is only suggestive at this time and while it has no practical value it deserves careful study, for some modification of technique may make it of diagnostic importance.

Heterolysins.—Kelling, whose theory of cancer origin has already been mentioned, has shown that serum of cancer patients is especially rich in heterolysins or substances that hemolyze the red blood cells of other animals. Because of his theory of cancer genesis he experimented with red blood cells of hens and has found heterolysins for those cells in 119 out of 265 cancer sera, while only 11 out of 320 non-cancer sera showed a similar property. He therefore claims that the presence of such heterolysins is almost specific for cancer. Many authors have confirmed the frequency of such hemolysins but have shown that it does not hold for the cells of hens alone, but is true for the cells of many other animals. It seems proved that cancer sera are especially apt to hemolyze such red cells but the reaction has not assumed any diagnostic importance, as such heterolysins are frequent in other diseases, and not as infrequent in normal persons as Kelling attempts to show. The reaction is of interest, however, as heterolysins for hens' cells were found in fifty per cent. of cases (357) and for sheep's cells in forty-two per cent. of cases (100) examined by various authors.

Antitryptic Test.—This test is based upon the fact that normal blood serum possesses to a high degree the property of inhibiting the specific digestive action of trypsin. Brieger and Trebing, following Markus, have found that in cancerous patients this property is very much increased, and have developed a simple technique for testing the relative antitryptic power of the serum. The technique roughly consists of exposing a Löffler plate to the digestion of mixtures of trypsin and of serum in different proportions, drops of the mixture being placed upon the surface of the medium. Normal serum usually inhibits any digestion of the medium and consequent "cupping" of the surface in proportion of 1 part of serum to 3 parts of 1 per cent. trypsin solution, while cancer serum is able to inhibit such action in proportion of 1 to 10, and even 1 to 20. Of the 584 cases of cancer reported upon by 20 authors the result was positive in 425 or 72.77 per cent. Pinkus has lately reported that he obtained positive results in 94 per cent. of 98 certain cases of cancer, while other observers report from 90 to 100 per cent. of positive reactions.

There seems to be no doubt that the antitryptic properties of the blood are very much increased in cancer. Moreover, it has been shown that this property diminishes after removal of the tumor, and increases again with the appearance of recurrent tumors. Its dependence upon the existence of the cancer seems, therefore, to be certain. However, it was soon discovered that other diseases are accompanied by the rise of the antitryptic property of the blood, namely, pneumonia, severe anemia, exophthalmic goiter, tuberculosis, nephritis with uremia, etc.,

and it occurs as frequently as in twenty-five per cent. of the cases examined. Indeed, the reaction is now spoken of as a "cachexia reaction" because it seems to accompany such a condition whatever be the specific disease responsible for it. Yet a positive result is of some value in case other diseases can be excluded; a negative finding is likewise somewhat reassuring, for non-malignant tumors are not accompanied by increase of antitrypsin. The technique of the reaction has been radically modified by other workers with it and its final value is still *sub judice*.

Anaphylaxis.—Pfeiffer and Finsterer think that in the course of cancer antibodies develop which induce anaphylaxis when injected into guinea-pigs. Guinea-pigs untreated or treated with normal blood serum show no reaction when injected with juice of cancer tissue. On the other hand, guinea-pigs injected forty-eight hours previously with blood serum of cancer patients and then injected with cancer juice display severe anaphylactic symptoms, among them the characteristic and easily determined anaphylactic drop in temperature.

The authors conclude that the serum of cancer patients contains anaphylactic bodies, and that the discovery of such bodies confirms the diagnosis of malignant disease.

Freund and Kaminer Reaction.—These authors have thought that the irregular appearance of metastases in cancer patients probably depends upon the properties of the blood serum which may inhibit the development of the neoplastic cells that reach the lymph or blood circulation. They have therefore examined the behavior of blood sera toward suspensions of cells derived from malignant tissue, and have found that, while normal sera destroy the cells, sera of cancer patients have hardly any such effect. The results of the reaction were estimated quantitatively by the use of a cell-counting chamber. Control experiments excluded any autolytic processes. Freund and Kaminer have varied their experiments in many ways, finally using simple extracts of cancer tissue instead of cell suspensions. They claim that cancer serum produces a precipitate when added to cancer extract while no such precipitate occurs with other sera. Methods employed by these authors are too technical to be discussed in this place but the important thing is the claim that both reactions are specific for cancer. Their conclusions have received some corroboration from the few authors who have tried the reactions in the short time since the publication of the technique.

Spontaneous Recovery from Cancer.—The characteristic features of cancer being persistence and tendency to growth the question of spontaneous recovery would seem to be opposed to the very definition of the disease. Yet cancers differ very much in the degree to which they exhibit the two characteristics mentioned above, and the chronicity of some of the well-authenticated cases, with marks of evident regression of tumors in other instances, make the spontaneous cure of cancer not *per se* an impossibility. Numerous instances of such recovery are, of course, found in the literature but only a few are supported by very strong evidence. Borst, the author of a noted treatise on tumors, thinks that all such reports depend upon a mistaken diagnosis in the first place. Williams cannot cite a single instance of "complete spontaneous cure" from his large experience.

Pearce Gould reported a case of a woman who had her left breast removed for a typical scirrhus, microscopically diagnosed, in 1880. In 1895 she was cachectic and showed numerous recurrent nodules in the skin, metastatic growths in the axillary and cervical glands, etc. Between that year and 1899 all these growths gradually disappeared and the patient improved in health; she was well until 1906 since when she has not been seen. He reports a similar instance in which the recovery from recurrent carcinoma of the breast took place after several years during which the patient appeared on the verge of death. Hutchinson, Broca, and others have reported similar cases. Czerny has lately shown that an operation with partial removal of a cancer may be followed by quiescence for years so that spontaneous recovery must be thought as possibly having taken place in such cases. It must always be remembered, however, that in many instances the very slow progress of the disease leads to the mistaken diagnosis of spontaneous cure; this was the case with Hodenpyl's patient in whom regression of many metastatic growths and general improvement was followed by death from internal metastases not diagnosed during life. In animal experiments, evidence of spontaneous cure has been noted by Gaylord and Clowes who reported a large percentage of spontaneous recoveries in mice they worked with; on the other hand, Bashford has seen but one case of this nature in 3,000 mice.

Treatment.—The only logical treatment of cancer at the present state of our knowledge is an early operation. The disease is local for a certain time of its development, and complete removal of the disease focus is the only method that promises cure with any degree of certainty. That such a statement is correct is shown by the increasing number of cancer patients who have successfully been operated upon and have continued to live without recurrence of the disease. The proportion of such persons has steadily increased with improvement in surgical technique and the spread of the conviction that to be curative the operation must be thorough, that is, it must result in the removal of all of the cancer tissue present. The reader is referred to the articles on the diseases of special organs for description of technique and the operative results recently obtained.

It is widely recognized now, however, that the old limit of three years, which was once thought to be sufficient to make sure that cancer has been eradicated, is altogether too short. Recurrences have taken place anywhere from a few months to twenty years after operative removal of the cancer focus, and while the longer periods are rather rare, intervals of three, four, and five years between operation and recurrence are common. Moreover, operation is often done when all hope of total extirpation is gone, when the local spread of the disease has reached parts that are inaccessible to the surgeon, or when metastasis into distant organs has already taken place. Such cancers, of course, speedily recur. Then, there are the great many cases that come for treatment when all hope for a successful operation is gone, the disease being in such a state as to preclude any benefit even from the extirpation of some troublesome local foci. There is therefore much need for non-operative treatment of cancer and while many methods have been used in the past and have been recently developed, the very multiplicity of them shows that none are specially successful.

Drugs.—Little need be said of the drug treatment of cancer. An enormous number of drugs have been recommended and have been tried and it may be said that none has proved of value in curing cancer, except in so far as some act as caustics and mechanically remove the cancerous focus. Arsenic alone deserves further mention because such authorities as Esmarch, Bilroth, Czerny, and others have reported favorably on its effects. It must be granted that in certain types of malignant disease, for instance, malignant lymphoma, arsenic appears to have some deterrent effect upon the rate of growth of the tumors. Of late, fairly favorable results have been obtained with such modern preparations as sodium cacodylate, atoxyl, salvarsan, etc. Any specific effect from these preparations, however, has not been noticed by competent observers (see below, under Chemotherapy).

Drugs, however, have a legitimate place in the treat-

ment of cancer from another standpoint, namely, to combat the numerous symptoms developing during the course of the disease. To repeat a trite statement, in cancer as in other diseases the patient and not the disease is the subject of treatment and all the mechanical, physical, and chemical therapeutical methods may find their logical indication in the treatment of patients suffering from cancer. Special care is needed to alleviate pain and the use of analgesic drugs is usually early called for. Reports from certain cancer hospitals give much praise to the newer coal-tar products when used for this purpose. Finally, however, morphine is usually called for, especially at bedtime to prevent a sleepless night when the distractions of daytime are not present to keep the sufferers' thoughts from their disease.

X-rays.—The use of *x*-rays now holds a well-founded place in the treatment of cancer. Hundreds of observations have shown that the rays destroy carcinoma tissue in the skin as effectually as any other mechanical or chemical method. Rodent ulcers are especially suitable for such treatment, occasionally in combination with operative removal of some portions of the growth. The advantages of *x*-rays consist in the painlessness of the method, in the absence of the ordeal of operation, and especially in the accessibility to treatment of lesions about the orbit, involving the eye, where operative removal is almost impossible. Pusey states that of 111 successive cases of skin cancer treated by *x*-rays, 72 per cent. showed successful results; of cases not incurable by other methods, practically 100 per cent. were successfully treated.

There is a fairly general agreement among surgeons, too, that *x*-ray treatment is of value in the prevention of recurrence after operative removal of tumors. The effects of the rays in cases of inoperable cancer are likewise favorable; pain is usually diminished, fetor very very much modified, sleeplessness often disappears, and the general state of the patient improves very remarkably. The rays of course do not cure the disease, but they certainly prolong life and, what is perhaps more gratifying, they make the life of the cancer patient more bearable because of doing away with the most unpleasant and annoying symptoms of the disease. It must be granted, however, that the mental effect of such a generally known and impressive agent as the *x*-ray probably has a good deal to do with the favorable constitutional effects that are frequently observed.

Radium.—Radium was discovered by the Curies, husband and wife, in 1898 and because of its wonderful properties soon attracted general attention. Its effects on the animal organism were early studied; on the skin exposure to it produces hyperemia, falling of hair, necrosis of the epithelium, ulceration, etc., effects which are similar to those produced by the *x*-rays. That it was not an indifferent substance so far as the general organism is concerned was shown by the production of convulsions, paralyses, etc., in mice exposed to its action, these symptoms finally ending in death. Of importance is its selective action upon the reproductive glands: it kills spermatozoa, leads to atrophy of the testicles and causes well-marked atrophy of the Graafian follicles in the ovaries.

It was soon shown that pathological tissue of any nature was destroyed by radium quicker than normal tissues. Apolant succeeded in curing mice inoculated with tumors, by the use of radium. Benign skin lesions, keloids, warts, lupus, psoriasis, were shown to be quickly affected by its emanations and in many instances were satisfactorily cured.

Czerny has made much use of it in the treatment of cancer. According to him cancerous ulcers may be healed, small tumors softened and made to disappear, and the general state of the patient's health much improved by the use of radium. Nahmacher used it in hope of preventing recurrences after operations and reports very good experiences with it although from the nature of the cases it is impossible to state how much good it has done. Finzi reports that complete local disappearance took place in twelve per cent. of ninety-nine cases of cancer treated by him with radium. Great relief from symptoms was secured in more than half the cases. He thinks that every local inoperable malignant growth should be treated with radium, and especially that every operation on cancer should be followed by exposure to radium as a prophylactic measure if the site is an accessible one.

Wickham who has had a great deal of experience with radium and has originated many ingenious methods of applying it, declares himself very cautiously. He treated over 600 cases, in this fashion, and states that there is no doubt that tumors may be arrested for months by radium and that occasionally they have completely disappeared, giving the impression of a real cure. Radium, however, acts only on localized lesions which are accessible or have been made accessible by operation. It diminishes the tumors, arrests secretion, and diminishes pain in advanced cases, and occasionally its use may make a previously inoperable cancer amenable to operative treatment. Butlin recognizes the value of radium but thinks that its use is not justified in any but the smallest-sized epitheliomata and in inoperable cases. He has never seen a case in which distant metastases were affected by applications to the original tumors. Einhorn has treated cancers of the esophagus and of the stomach by radium, having devised special receptacles by means of which the radium tubes can be brought into contact with the tumors. In cancers of the esophagus he has seen improvement in most cases, malignant strictures often becoming passable; the patients felt better, could swallow better, and suffered less from pain. He saw some palliative effects in the few cases of cancer of the stomach he has treated in like fashion.

Abbe of New York has treated numerous cases of cancer, mostly sarcoma, with radium and has obtained favorable results in many instances. As a rule recession of tumors was noted in most cases and in a few the tumor disappeared completely. Thus, a round-celled sarcoma of the eyelid disappeared after four exposures to radium, no recurrence being noted in three years; an extensive giant-celled sarcoma of the jaw which disappeared under radium, did not recur in the four years of observation.

Cancer Ascitic Fluid.—In the year 1910, the late Eugene Hodenpyl of New York reported the case of a woman who suffered from numerous recurrences in and about the operative scar after removal of the breast for cancer; she also had secondary tumors in the other breast and in the neck. She developed metastases in the liver, which led to the formation of ascites. Gradually, the recurrent and secondary tumors disappeared, the liver became smaller, and the woman's general condition became very much improved. She, however, had to be tapped frequently to relieve her of recurrent ascites. Hodenpyl conceived the idea that the patient must have developed some antibodies to cancer and that the ascitic fluid perhaps contained these substances. Experimental use of the fluid was very gratifying, tumors in mice being favorably affected. Hodenpyl then tried the fluid in human cancer patients, giving it subcutaneously and intravenously in large amounts. He reported fair success.

Hodenpyl's report led to a wide trial of ascitic fluids from cancer and other patients in the treatment of malignant disease and most of the observers noted some temporary improvement in the cases treated. Prolonged trial, however, led to complete disappointment. Risley used several kinds of body exudates and transudates in forty-five cases of cancer over a period of seven months. He concludes that cancerous ascitic fluid has no permanent effect in preventing or checking the growth of cancer of active or fairly

resistant type, though temporary beneficial results may be noted for periods of from one to five months. The course of the disease is in no way permanently retarded. In a small percentage of cases Risley saw temporary relief from pain, especially in cases of cancer of the uterus. In one patient with cancer of the ovary her own ascitic fluid was used and some benefit was noted.

Weil studied various ascitic fluids and was unable to find by any chemical or biological test any antibody or specific substance which differentiated them from each other. It must be concluded that while failure has so far followed the use of the method of treatment suggested by Hodenpyl, so far as cure is concerned, the unmistakable though usually very temporary improvement that has been noted in many cases shows that this method should not be abandoned without further study. While it may not lead to any "cure" for cancer it may explain the varying rate of rapidity with which cancer develops in different individuals.

It should be noted that Hodenpyl's patient finally died of cancerous metastases, which were not recognized during her life but which were discovered at the autopsy.

Fulguration.—This method of treating inoperable cancer has been used by de Keating-Hart since 1906 and recently has led to a great deal of discussion, as to both its mode of action and its alleged results. Although the method is described by many authors as simple destruction of cancer tissue by means of a high-frequency spark obtained from a special apparatus, de Keating-Hart claims that such destruction, when it occurs, is harmful and is not true fulguration. The latter consists of overstimulation of tissue by the current which acts more upon cancer soil than upon the cancer itself.

Whatever the nature of the method, it was first hailed with great enthusiasm. Czerny was at first a very warm advocate of the method, having observed most gratifying results. He used it in connection with surgical removal of cancer tissue, fulgurating the wound in the hope of preventing recurrence. Later, he became somewhat cooler toward this method, though he still grants that it is of great assistance and gives in thirty minutes results that are equivalent to those obtained with *x*-rays or radium in three months. In general it is granted that cancers treated by the de Keating-Hart method are frequently followed by local healing, where this would not be probable with other methods of treatment. It should be used in cases where operation is necessarily incomplete, and some authors think that it could advantageously precede treatment with the *x*-rays or radium. That is it not a "specific" method of treating cancer has been further shown by the fair success met with in using it for the treatment of certain other chronic affections (tuberculosis of the skin, etc.).

Various other methods of electrothermic destruction of cancer tissue have been tried in recent years and while some of them have been shown to be a better way of dealing with cancer tissue in places where the knife or the actual cautery is contraindicated or difficult to use, none has been shown to have any specific merit in its effects upon cancer tissue. Quite recently de Keating-Hart has experimented with the use of fulguration and of *x*-rays on tissues the temperature of which has been artificially raised, while the skin and any organ which is to be protected from the destructive action of the rays are artificially cooled. To this method the term *thermoradiotherapy* has been applied. Independent conclusions about its merits have not yet been reached.

The Enzyme Treatment of Cancer.—Under this title is understood the employment of trypsin and amylopsin which was founded on certain embryological theories of John Beard and for a long time awakened much hope. Trypsin was found to have a liquefying effect upon tumors, and small ones have been made to disappear by injections of the enzyme. Most observers, however, have reported complete failures so far as "cure" of infiltrating cancer or one that has already given rise to metastatic growths is concerned, even when all regard has been taken to combine injections of amylopsin with those of trypsin as urged by Beard. There exist, however, several favorable reports on Beard's treatment of cancer and the reader is referred to that author's latest book on the subject (The Enzyme Treatment of Cancer and its Scientific Basis, by John Beard, London, 1911). So far as extended use of these remedies is concerned a perusal of the more recent medical reports on the treatment of cancer seems to show that they have generally been given up.

Opotherapy.—It may be mentioned in this connection that since the time of Brown-Séquard extracts of animal organs have been used in the treatment of cancer. The originator of this form of therapy himself reported upon the good effects noted in several cases following the administration of testicular extract, his pet preparation. Beatson advised removal of ovaries in women suffering from breast cancer and in addition administered thyroid substance. Thyroid has been quite extensively tried in the beginning of this century and has certainly shown a certain influence upon the growth of tumors, especially upon metastatic growth in the lymph nodes. Malignant disease of the larynx has likewise proved somewhat susceptible to this preparation, several cases having been reported where complete disappearance of the tumor has taken place. Recurrence, however, has usually been noted. There are several cases in which the period of freedom from recurrence after the treatment with thyroid has been several years. Extract of thymus gland has likewise been used with about the same results as with thyroid substance. Von Leyden and Bergell have used a proteolytic ferment derived from animal livers and have witnessed remarkable destruction of cancer tissue under its employment, that led to untoward symptoms of intoxication. They have not obtained any very remarkable therapeutic results.

Chemotherapy.—The remarkable success of Ehrlich's salvarsan has led to several attempts to discover or prepare substances that would have a specific affinity for cancer cells. The first report of a chemical of such nature was published recently by Wassermann and coworkers, the substances examined being salts of selenium, which have previously been shown to be very readily reduced by growing cells. Cancer cells, because of their increased growth energy, were found to be specially capable of reducing the salts and precipitating selenium *in vitro*. In the animal body, however, selenium proved to be as destructive to the cells of the organism as to the cancer cells, and it therefore occurred to Wassermann to combine selenium with eosin, the latter having the property of being rapidly distributed in the body, thus reaching cancer cells before much damage has been done elsewhere.

Experiments with tumor-bearing mice showed that the selenium was deposited in the tumors and led to softening, which was followed by absorption of the tumor masses. The mode of death of the tumor cells was shown by Hansemann to be very peculiar, nucleolysis being the first step in the destruction. The curative and toxic doses of the preparation were, however, found to be very near each other, and death occurred in many of the mice treated; the products of destruction of the tumors likewise proved to be very dangerous.

Neuberg and Caspari have reported somewhat similar results with other chemical substances, their work being founded not upon the increased growth energy of cancer cells but upon the well-known tendency of these cells to necrosis and death. These authors have used colloid metals, leading to autolysis

of tumors and resulting cure. Quite recently Loeb has shown that colloid metals may be used with advantage in the treatment of human cancers, when administered by the intravenous method.

Serotherapy.—Richet and Hericourt were among the first to apply the principles of serotherapy to cancer. They injected animals with preparations of cancer tissue and then utilized the serum of such animals in the treatment of cancer. They witnessed favorable clinical results: diminution of pain, better sleep, better appetite and digestion, and general improvement. The tumors seemed likewise favorably affected, hemorrhages becoming rare, ulcerations cleaner, lymph nodes smaller in size.

Since their time, numerous attempts have been made to produce an active or a passive immunity against cancer. A great variety of procedures have been developed: sera of normal animals, supposedly immune to cancer; sera of animals immunized against embryonal tissue, against cancer tissue, against various microorganisms some supposedly holding an etiological relation to cancer, others having no such relation; finally vaccines, consisting of tumor tissue of the patient, of tissue of other tumors similar or different in character—all these and many others have been tried in sequence and the literature of this form of treating cancer is becoming more and more voluminous. It may be said that almost all of the attempts have resulted in some isolated cases in which improvement, local or general, has been witnessed; a few of the procedures have to their credit one or two alleged "cures," inoperable cancers having disappeared and not having recurred for a certain period of time; none of them however proved to be curative in any general sense.

Great hopes were aroused for a time when Jensen reported that it was quite possible to prepare a cytolytic serum for animal cancer. He injected rabbits with emulsion of mice tumor and cured other tumor-bearing mice with the resulting serum. These results have been questioned, spontaneous recoveries being not infrequent in cases of mouse tumors. Vidal has made a careful study of cytolytic sera and after numerous modifications of technique has succeeded in effecting at least three cures in cases of inoperable cancer in a total of almost one hundred cases tried. One of the patients had an epithelioma of the tongue and was alive, with cicatricial contraction of the tongue, seven years after treatment; another case was that of cancer of the rectum, the patient being alive seven years after the conclusion of treatment; the third was cancer of the breast, the patient living ten years after treatment. Several other cases have been much benefited, in some operation becoming possible after the use of vaccines.

At the present time the study of the rôle of vaccines and sera in cancer therapy is going on in the hands of many workers and their final value will probably be soon settled, especially as attention is now being directed to the principles of all such treatment rather than to this or that modification in the preparation of the therapeutic substances.

Coley's Fluid.—In studying, over twenty years ago, cases of sarcoma at the New York Hospital, W. B. Coley ran across a case of very malignant round-celled sarcoma of the neck, four times recurrent, during the course of which the patient suffered two attacks of erysipelas. During these attacks the tumor disappeared entirely and the patient left the hospital. Coley found him alive and well in 1891, seven years afterward. This induced Coley to try artificial inoculation with erysipelas and finally to use the toxins of the streptococcus from cases of erysipelas, first alone and then in combination with the toxins of *Bacillus prodigiosus*, in the treatment of malignant disease and especially of sarcoma.

In a late review of personal results and of those reported in the literature he tells of having had success in 42 cases of malignant disease out of some 500 cases treated; of these 17 were round-celled sarcomata and an equal number of spindle-celled sarcomata. The remaining tumors were of mixed type or were not pathologically examined, and one was an epithelioma. Of these patients 21 were well from five to fourteen years after treatment, 26 well from three to fourteen years, and 10 were well ten to fourteen years after treatment. He thinks that successes reported by other authors add up to about 100 cases.

Roughly then, Coley claims to have had success in about ten per cent. of cases, for he has reported numerous successes since his last comprehensive paper on the subject. One or two of the cases have been malignant tumors of epithelial nature. Notwithstanding these reports it is not exaggeration to say that the profession in general has been undecided as to the rôle of Coley's toxins in the treatment of sarcoma. That such attitude exists is best evidenced by the tone of Dr. Coley's papers in 1906 and again in 1907 in which he recounts the above results and pleads for recognition of the toxins as a remedy to be tried in the treatment of inoperable sarcoma and in the prevention of recurrence after operation, and even before operative interference in certain cases. Of course, the usual conservative attitude of the profession toward cancer "cures" in general is one element in this attitude toward Coley's toxins, another one depending upon the change in reasoning which led Dr. Coley to adopt his present method of preparing toxins. Starting from the cure of malignant disease by erysipelas, and in this he is supported by other observations as we have seen, he has added to his fluid the toxins of *Bacillus prodigiosus*, an organism that is probably not pathogenic for human beings, and therefore one that never had anything to do with spontaneous cure of cancer. Indeed, Dr. Coley lays special stress upon the use of the mixed toxins especially accentuating the effect of *Bacillus prodigiosus* which apparently is the most important element in the fluid. Of course, this does not destroy any evidence as to the value of the fluid, only with it there disappears any logical connection between the recovery seen after erysipelas and the use of Coley's toxins. The treatment becomes toxin treatment purely and there is no special virtue in the erysipelas part of the argument. As a toxin treatment Coley's fluid deserves further study for there is no reason why the principle of such treatment should not be carried out as well and better by other combinations than that devised by Coley.

Doyen's Vaccine.—This surgeon claimed to have found the causative organism of cancer in *Micrococcus neoformans*, which, according to him, is constantly present in malignant tumors, both primary and metastatic. Cultures of the organism produced tumor-like structures in various animals. Doyen prepared vaccines of this organism, attenuated by exposure to heat and admixture with arsenic, and has recently (1904) claimed to have cured 42 out of 242 patients treated, and markedly benefited others. As usual, a flood of conflicting reports followed Doyen's publications. In France a committee of the Society of Surgery was entrusted with trial of the new remedy, and its president, Delbet, issued a very adverse report, none of the twenty-six cases in which Doyen's vaccine was tried having been benefited. Recently Jacobs and Geets have applied Wright's principles to the preparation of vaccines from Doyen's micrococcus and have published fairly favorable results. The consensus of opinion, however, seems to be that any good effects of Doyen's vaccines are due to the various hygienic and medical means he combines with his treatment, as well as perhaps to the beneficial effects of the toxin of his organism. Any specific relation of *Micrococcus neoformans* to the genesis of cancer has not been shown; whether or not it may be held responsible for some of the accompanying symptoms of

cancer, such as anemia, cachexia, etc., in some cases, is still a moot question.

Antimeristem (*Cancroidin Schmidt*).—This preparation must be noted because of its frequent mention in cancer literature. Schmidt claims to have isolated an organism of protozoan nature from malignant tumors with which he has produced alleged tumors in animals. He has also used a culture of the organism in the treatment of cancer and has reported numerous alleged successes. The preparation is now on the market under the name "Antimeristem." Other observers have noticed some fleeting improvement in several cases treated with this preparation, but all deny it any specific action. Its use may be classed among the treatment of cancer with toxins.

Cultures of Blastomycetes.—Sanfelice has been the most enthusiastic and consequential student of the relation of blastomycetes to cancer. He claimed to have isolated the yeast species causative of cancer (*Saccharomyces neoformans*) and with it to have produced neoplasms in animals. Moreover, by injecting dead cultures of the organism he has obtained fairly powerful protective and even curative sera. Wlaeff has prepared a serum of like nature with which he treated some sixty cases of human cancer; he claims to have cured several cases in which dissemination had not already taken place. Recent researches have shown that blastomycotic infections are not at all rare in animals and in human beings, and they result in granulomatous lesions which are strictly inflammatory in character. The yeasts found in tumors are probably secondary infections and certainly they cannot be looked upon as the cause of cancer, or even suitable for the manufacture of any sort of antiserum for the treatment of malignant disease.

Conclusion.—It may be concluded that the problem of cancer has lost its narrow medical interest but has become of significance to humanity in general, because of both the practical importance of the great scourge and the vast scientific interest involved in the discovery of its cause and of methods of protection against it. Recently marked advance has been made in dealing with the cancer problem, first, by the establishment of cancer research institutes which offer all the necessary surroundings for carrying on experimental study of cancer and cancer-like diseases of lower animals, as well as for special examination of the pathological material obtainable from human cancer patients; in the second place, it has become understood that the physician's interest in the cancer patient does not end with the operation, but that he is to be looked upon as suffering from a disease of varied duration and phenomena which require just as careful observation as typhoid fever or tuberculosis, for instance. This attitude has lessened the tendency of inoperable cancer patients to seek aid in the hands of quacks and charlatans, and on the other hand has taught the physician that in a chronic disease like cancer much can be done to alleviate suffering and to prolong life, however hopeless may be the ultimate prognosis. Any one who has watched the mental condition of inoperable cancer patients undergoing treatment could not have failed to notice the favorable psychic effect upon such patients of the consciousness that orthodox medical science has not given them up, and however baffling their illness, everything possible is being done to overcome it. The treatment of inoperable cases of cancer thus becomes a distinctly medical problem and it may be hoped that with time the great hospitals that now refuse admission to such sufferers will see the way clear to their accommodation, partly in the general wards where intercourse with other patients may lead them to a more cheerful attitude of mind, and partly in special cancer wards where all effort is being made to lay bare the mystery of the nature of cancer and perhaps lay the foundation of future effective treatment.

Many years ago—in 1773—the Academy of Lyons awarded a prize to one Bernard Peyrilhe for the best essay on the subject "What is Cancer?" Peyrilhe said: "Cancer is a malady just as difficult to define as to cure!" It cannot be denied that notwithstanding the great amount of work done since Peyrilhe's time this conclusion is as valid now as it was at the time it was uttered. Yet a vast number of facts have been added to our knowledge of cancer, and the accelerated *tempo* of cancer research witnessed in the last ten years justifies the belief that still more important and fundamental information may become our property in the very near future. As MacCallum has said, "The last ten years have contributed marvellous things. The next ten years may tear aside the whole veil."

B. Michailovsky.

Cancer, Pathology.—See *Carcinoma and Sarcoma.*

Cancrum Oris.—See *Gangrene.*

Canella Bark. N. F.—*Canella Alba. Wild Cinnamon.* The bark of *Canella winterana* (L.) Gaertn. (fam. *Canellaceæ*) deprived of its corky layer and dried. It is a native of the West India Islands, especially of Jamaica, Cuba, and the Bahamas, and also of the southern part of Florida. The bark of this tree was first made known in Europe in the early part of the seventeenth century, and since then has been in continuous but very limited demand. It has been frequently confounded with Winter's Bark (*Drymis winteri* Forster), and with *Cinnamodendron corticosum* Miers. It is now very little used excepting in its home, where it is highly esteemed, more as a condiment than as a drug.

It comes in broken quills, sometimes thirty or forty centimeters long and 0.5 cm. thick (12 to 15 in. by ¼ in.), but averaging much smaller. The outer surface is roughish and bright buff-colored, the inner smooth or finely striated, yellowish or creamy white; fracture short and granular, odor rather agreeable, cinnamon-like; taste pungent and bitter. It contains numerous large oil cells, especially in the outer portion.

The leading constituent is the *essential oil*, of which it contains from three-fourths to one per cent. and which contains eugenol and cineol; tannin is absent. A considerable percentage of mannite can also be separated. The bitter principle needs further study. Canella is a stimulant tonic, similar to other aromatics, over which it appears to have no other advantage than the possession of a bitter principle. It is not poisonous, and is seldom given alone, in doses of gr. viii. to xxx. (0.5–2.0). H. H. Rusby.

Canities.—This condition of *grayness of the hair* may be congenital or acquired, partial or complete.

Congenital canities usually occurs in the form of tufts of white hair, but may occur as round patches. This form of canities is rare. In some families it is hereditary, a white tuft of hair occurring in a large number of their members. General congenital canities is part of that general absence of pigment that is known as albinism.

Acquired canities is the form most often seen. It usually begins at about thirty-five years of age, but in some families and under certain circumstances it may begin much earlier. Beginning in early life, it constitutes premature canities; beginning at middle life, it is one of the changes incident to growing old. Few people reach fifty years of age without some gray hair.

The hair on the temples is most often that which first changes color, though there is no definite rule as to where the disease first appears. The beard may be first affected, but usually it is affected secondarily to the scalp hair. The pubic and axillary hair may escape all change in color, though at least they, too, generally are affected. When once grayness begins it is slowly or rapidly progressive. Exceptionally

and rarely the normal color may return to gray hair, just as it is possible to have a third set of teeth. The change in color takes place first at the root of the hair. As the pigment becomes more and more deficient the color of the hair slowly changes from gray to a creamy or snowy white. In most cases the change in color is the only change that the hair undergoes Alopecia may set in, but it bears no definite relation to change in the color of the hair.

Too many well-authenticated cases are now on record to allow of doubt as to the sudden occurrence of canities—over night in some cases. Such instances are almost always in relation to severe mental shock, such as the reception of some fearful intelligence.

Ringed hair is a peculiar and rare form of canities in which the hairs are marked by alternate rings of white and normal color. The diameter of the hairs is unchanged. The white rings are narrower than the colored ones. Very few of these cases are on record.

Etiology.—Canities is due to an interference with the pigment formation in the hair papilla. Metchnikoff believes that the loss of pigment is due to the phagocytic action of certain cells which he designates as pigmentophages. These are round or oval cells with prolongations. When the hair begins to turn gray certain cells of the medulla become mobile, penetrate into the cortex of the hair, and there absorb by means of their prolongations the pigment granules. They then descend with the absorbed pigment into the matrix pass through the epithelial layers of the bottom of the follicle, and into the adjacent connective tissue. The gray color is the combined result of a deficiency of pigment, the presence of air bubbles between the cells of the cortex, and the essential color of the hair. When the hair is white there is no longer any pigment in the hair. The occurrence of sudden blanching of the hair is due to the entrance of air bubbles between the cortical cells. That air between the cells is one factor in causing a gray color is shown by placing a gray hair under the receiver of an air pump and exhausting the air. It will be seen that the hair regains its normal color to a greater or lesser extent.

Age, heredity, nervous shock or strain, neuralgia, injury to the scalp, and all debilitating diseases, are predisposing causes of canities. There is no adequate explanation for the occurrence of ringed hair.

Treatment.—Nothing can be done for most cases of canities. If it is due to some removable cause the color may return when the cause is removed, but no promise of this should be made. Jaborandi and acetic acid seem to have some influence on the color of the hair, and may be tried, the first internally and the last externally. Hair dyes should never be advised. Once used they must be persisted in. Many of them are harmful, especially those containing lead.

George T. Jackson.

Cannabis Indica.—*Indian Cannabis. Indian Hemp.* The dried flowering tops of the pistillate plants of *Cannabis sativa* Linné (fam. *Moraceæ*) deprived of thick stems and large leaves, and containing not more than ten per cent. of mature fruits.

Cannabis sativa is indigenous to Central Asia, but has been cultivated throughout Europe and America for its valuable fiber, from which hemp is manufactured, and for its seeds and their oil. It is a large, very variable, annual herb, with an upright, slender, usually branching stem from one to three meters high (3 to 10 feet). In the female plant, the flowers are in small, erect spikes, each in the axil of an upright, pointed bract, consisting of a single one-seeded, two-styled carpel enveloped in a broad, spathe-like, one-leaved perianth. Fruit (the hemp seed of commerce), a roundish-pointed achenium containing a single pendulous, oily seed.

The plant contains a large amount of resin, which exudes upon the surface, more particularly upon the flowering branch. This resin becomes most abundant at the beginning of fructification, and as the fruit forms it diminishes in a very marked degree. Under cultivation, any such loss of resin is prevented by eliminating the male plants or by gathering the tops before the fruit begins to form. In temperate climates

Fig. 1188.—Pistillate Inflorescence of the Hemp Plant. (Baillon).

the plant is deficient in resin, and for medicinal purposes that which is grown in India and Southern Asia is very superior.

Indian hemp is collected in three forms: first, the flowering tops of the female plant, known as "gunjah," secondly, the leaves, "bhang," which are used for smoking; and, thirdly, the resin, "churrus," or "charus," which enters into the composition of "hashish," and is also used for smoking.

The tops as they reach us consist of compressed masses of branches and leaves with flowers, and at times with specimens of immature fruit, the whole matted together by the resinous secretion. The leaves and bracts bear external oleoresin glands, and one-celled curved hairs, which are very characteristic and serve to identify the plant. The bases of these hairs are enlarged and frequently contain cystoliths. The tops have a greenish-brown color, a narcotic odor, and a slightly acrid taste. The medicinal value of the plant varies greatly and is very uncertain. This, in a measure, is due to climatic influence and the period of collection; but it is also accounted for by the time that has elapsed since the plant was collected and by its mode of preservation. Experiments have shown that the plant diminishes in strength, after a period of six months, when exposed to the air; while control specimens, which are kept in air-tight bottles, still remain active. A gradual oxidation of the resin is the supposed cause of the change.

Our knowledge of the active principles of the plant remains very uncertain. The resin as originally separated by T. and H. Smith, of Edinburgh, in 1846, and named *cannabin*, is still accepted as representing the active principles, and is almost entirely employed for medicinal purposes. It forms the solid extract of the Pharmacopœia, and the fluid extract and tincture are alcoholic solutions. In 1857, Personne described *cannabene*, a volatile oil, which for some time was thought to be the active ingredient. It has, however, proved to be an impure sesquiterpene, and of no therapeutic value. An alkaloid resembling nicotine has been found at different times, but it never has had the characteristic action of cannabis.

Cannabis indica was very thoroughly studied by Professor Marshall and his assistants, in his laboratory at Cambridge University. As an outcome of their investigations there was produced a red oil to which they gave the name of *cannabinol*, and the chemical formula $C_{18}H_{24}O_2$. This they considered to represent the active properties of the plant, but the comparative therapeutic value of the compound is as yet uncertain.

Cannabis indica is much used by the natives of India, Arabia, and neighboring countries as an intoxicant. For this purpose the dried leaves and the resin are smoked, either uncombined with other ingredients or mixed with tobacco. In Arabia the resin is combined with opium and other narcotics to form the well-known "hashish." In some instances a decoction is made from the leaves and employed as a beverage to induce the intoxication. The effect produced is an inebriation of an agreeable character, exciting the individual to sing and laugh. There are pleasant and often gorgeous visions and hallucinations, with a sense of ecstasy, and more or less delirium, terminating in a deep sleep. The sleep may be cataleptic in character, the muscles being slightly contracted and the limbs pliable. Later observers have described a condition resembling hypnotism. During the intoxication the sexual propensities of the individual are stimulated, which has established its reputation as an aphrodisiac.

Fig. 1189.—Staminate Inflorescence of the Hemp Plant. (Baillon).

The craving for this stimulant is very prevalent among the Asiatics, and many who are addicted to its use are more or less continually under its influence.

The effect produced by cannabis indica varies according to the mode of administration. When the fumes are inhaled it is a stimulant and intoxicant. Its effect begins early, and if but a small amount is used, it passes off in half an hour or more. If it is taken into the stomach its action is slow, an hour or two elapsing before the drug is absorbed. In this way its stimulating effects are much less marked, and its depressant and narcotic action is more evident. As an anodyne and antispasmodic it is classed by many as ranking next to opium. In large doses it produces the same effect as when inhaled. Experimental work has shown that the primary stimulation rapidly passes and is followed by depression, loss of reflexes, ataxia, diminished sensibility, a tendency to sleep, and stupor, with a certain degree of anesthesia and paralysis. The effect upon the heart and respiration is not a prominent symptom. The early stimulation continues for some time, and the depression of respiration and circulation becomes marked only as narcosis begins. The mode of death is uncertain, some observers reporting that death takes place from cardiac failure, while others state that the heart was observed to beat after the respirations had ceased. Upon the kidneys it exercises no direct action, but the tendency is to increased excretion of urine. It is stated that a decoction of the fresh plant is an active diuretic. No specific action upon the sexual organs has been detected, excepting that accompanying the general stimulation. Cannabis indica is not a dangerous drug. The physiological effects may be very marked, but to cause death a very large amount would be required. No authentic instance of its fatal effects has been recorded. In animals it is found that, of the fluid extract, ♏ x. (0.6) will cause marked symptoms, but as much as ℥i. (30.0) is required to produce death.

The therapeutic value of Indian hemp is due to its influence on the nervous system, and by some it is supposed to act directly upon the cerebral cells. Its sedative effect is most valuable in functional disorders and in pain not due to inflammation. It has proved of value in the aged when the mental faculties are weakened generally and when much restlessness and sleeplessness are prominent symptoms. In doses of gr. $\frac{1}{4}$ to $\frac{1}{3}$ (0.015–0.02) at bedtime a calm and quiet sleep is secured, and the same action may be secured for weeks without increasing the dose. In melancholia and chronic alcoholic delirium of the aged, accompanied by depression, it has acted as an exhilarant, has produced the desired sense of strength, and has secured quiet and rest. In the restlessness of general paralysis and "temper diseases," in both adults and children, it has also been of the greatest service.

In painful maladies it has acted best in those of a functional character, such as neuralgia and migraine, either alone or when combined with constitutional remedies, as iron, quinine, and zinc, when such are indicated. In neuritis it proves of service only when given in addition to mercury, iodine, and other such remedies. It has also proved very serviceable in the formication, tingling, numbness, and other sensory disturbances of the elderly and gouty.

It has been very successful in clonic muscular spasms such as the convulsions of children and adults due to reflex causes, in epileptiform convulsions due to organic disease of the central nervous system, and in cases of brain tumor accompanied by convulsions and other indications of central irritation. In true epilepsy it has proved useless. In numerous cases it has been given for a prolonged period until its full physiological action was produced, and yet it has failed to influence the disease in the slightest degree. It relieves the distress of spasmodic asthma and has proved very serviceable in spasmodic dysmenorrhea not associated with metritis or with other inflammatory affections. It has proved of service in chorea, whooping-cough, hysteria, migraine, and neuralgia. It has also proved of particular usefulness in painful disorders of the stomach, when not accompanied by organic changes. It has proved a better sedative than opium, as it exercises hardly any derangement of the secretions. Its beneficent effects are increased by attention to the state of the secretions, and by the employment of alkalies, purgatives, and other stomachic drugs when such are indicated.

In administering this drug the great drawback has been the unreliability of the various preparations. To obviate this, it is advisable to restrict one's practice to the use of a single preparation, beginning with a moderate dose and gradually increasing until its physiological effect is produced. Notwithstanding the various active principles that have been described, the resin and its preparations are much to be preferred. Physiologically standardized extracts, both solid and fluid, are now carefully prepared, and either these or the tincture should be employed. The dose of the solid extract is from gr. $\frac{1}{4}$ to gr. i. (0.015–0.06), that of the fluid extract is from ♏ ss. to ♏ i. (0.03–0.06). The advantage of the fluid extract is supposed to be due to the fact that only moderate heat is employed during its preparation. The average dose of the ten-per-cent. tincture is ♏ x. (0.6). The preparations should never be added to aqueous solutions as the resin immediately separates as an insoluble mass.

Beaumont Small.

Cannani, Johannes Baptistus.—Born at Ferrara, Italy, in 1515. He occupies a position of considerable

distinction in the history of anatomy. He was a disciple of Brasavola, and subsequently taught anatomy with great success at the University of his native city. He was first physician to Duke Alphonso II., and afterward served Pope Julius III. in the same capacity. He died at Ferrara in 1578, in his sixty-third year.

Like Vesalius, Cannani was careful not to follow blindly the anatomical descriptions given by Galen; instead, he went direct to nature for information with regard to the relations of the different parts. It is from Amatus Lusitanus and Fallopius, his contemporaries, that we learn the fact that Cannani was the discoverer, in 1547, of the valves of the renal, primitive iliac, and azygos veins. A. H. B.

Cannes.—Cannes, a winter resort on the French Riviera, is picturesquely situated in a recess of the Gulf of Napoule. It is 660 miles distant from Paris, 120 from Marseilles, 19 from Nice, and 28 southwest of Mentone.

It is well protected on the east, and partially so on the west, by an isolated mountain group called the Esterel. On the north, however, the higher ridges of the Alps are too far distant to afford proper shelter. Like Nice it is a windy place, the sharp, violent, and disagreeable *mistral* (northwest wind) prevailing frequently in February and March. It is less sheltered than Mentone and San Remo, and consequently the climate is less equable. The general characteristics of the climate of this resort are mildness, abundant sunshine, moderate average rainfall, and, for the seashore, a low relative humidity. The winds and the lack of equability, particularly between the sun and the shade and the day and night temperatures, are some of the objectionable features. "The Riviera," says Burney Yeo, "is a land of sunshine and a land of winds. It is a land of intense, brilliant sunshine and of cold, chilling shade." "The deceptive combination," says Lindsay, "of brilliant sunshine with cutting blasts is the great climatic defect of the Riviera." The great and continued popularity of this, as well as of the other resorts of the Riviera, depends not so much on the intrinsic excellence of its climate, as on its comparative superiority over the usual climate of the more northern portions of the Continent and of England. Climates like pleasures are often judged by comparisons, and when, for instance, we compare the winter climate of London or Vienna with that of Cannes, the latter appears quite superlatively excellent. But if we compare the climate of Cannes with that of some resorts on the opposite coast of Africa or in Southern California, or with that of many of the resorts in our Southern States, Cannes decidedly suffers by the comparison. When, on the other hand, one considers the beauty of its situation, the variety and charm of its scenery, the richness of its vegetation, and all the fascination incident to a resort on the beautiful Mediterranean coast, Cannes surely has few superiors. It is to be borne in mind, say Burney Yeo and others, that at Cannes one can avail himself of two somewhat different climates, according as he chooses a residence in the neighborhood of the seashore or inland in the valley of Cannet, for example, about two miles distant from the sea, where greater protection for dwellings and promenades is afforded. All writers upon the latter climate refer to it as "bracing" and "exciting," with a tonic and stimulating atmosphere.

The following meteorological table arranged from Marcet's personal observations, extending over a period of from two to six seasons ("Southern and Swiss Health Resorts," by W. Marcet, M. D.), will give the reader a means of comparing this with other climates. The data are for the winter season, extending from November to April inclusive:

The climatic characteristics of the various months are summarized by Marcet as follows: "In November and December the weather is usually stormy and wet. January and February are fine, with occasional visits of the dry northwest winds. During these two months the air is usually calm in the morning with a pleasant light southerly breeze blowing in the afternoon, while a northerly land breeze commences at sunset and is continued during part of the night. March and April are windy and showery, the winds showing no particular regularity, although in general easterly with wet weather." "At night," continues Marcet, "there is a sudden accession of cold together with the increase of atmospheric moisture at sunset and continued at night; therefore the importance of the invalid being indoors before sunset." Fogs are unknown, and there is an absence of mist. Occasionally the temperature sinks to the freezing-point, and snow sometimes falls. As almost everywhere else, occasionally the unexpected happens, and a very wet or very cold season occurs, "and then," says Burney Yeo, "the sufferings of the visitors are very acute, much more so than at home." There is a considerable amount of lime in the soil, which adds to the disagreeable effect of the dust, which is always an annoying feature.

Dr. J. Henry Bennet wisely warns the visitor not to expect perpetual spring or eternal summer in the Riviera. The Riviera is not Southern California, and

Climate of Cannes, France Fahrenheit Scale.

	November.	December.	January.	February.	March.	April.	Season.
Temperature—							
Mean average temperature	52.6	46.3°	48.0°	48.8°	51.0°	55.5°	50.8°
Average daily range	12.3	12.4	12	13.4	13.2	12.8	
Mean of warmest	58.8	52.5	54	55.5	57.6	62	
Mean of coldest	46.5	40.1	42	42.1	44.4	49.1	
Mean maximum sun temperature	99.7	91.6	96.1	106	114.7	120.7	
Mean lowest night temperature	38.4	31.4	32.2	33.8	35.4	41.9	
Precipitation—							
Average in inches	5.17	4.51	1.69	1.46	3.42	4.05	20.31
Wind—							
Prevailing direction					W.	E.	E. and S.E.
Calm days	10.7	11.7	12.5	8.2	3	2.7	48.8
Light to fresh	12.7	13.5	13	11.7	19.2	18.5	88.9
Stormy to gale	6.2	5.7	5.5	7.2	8.7	8.5	41.8
Humidity—							
Average relative	71.2	72.7	71.7%	75	73.1	74.3	73
Weather—							
Fine days	17.5	18.8	21	20	21.3	18.4	117
Overcast	2.1	3.5	3.8	3.1	2.6	1.5	16.6
Rainy	9.5	8.8	6.3	5.3	7.1	8.6	45.6
Temperature of sea	61°	57.1°	55.7°	55.5°	56.7°	59.3°	

a climate similar to that of the latter region must not be expected. If the reader will turn to the article upon *California, Southern,* in this volume and compare the climatic tables of San Diego and Santa Barbara with that given here of Cannes, he will realize the difference. For instance, the average mean temperature for January at Cannes is 48° F., while at San Diego it is 53.6° F., and at Santa Barbara 51.2° F. Further, the rainfall at these two California coast resorts is only about half of what it is at Cannes, and the number of fair and clear days is considerably greater, and there is also less wind. Although the relative humidity is almost exactly the same, the complete absence of fog would seem to indicate a comparatively drier atmosphere at Cannes.

It is well to emphasize again the fact of the winds; they are the *bête noir* of Cannes, as indeed of the Riviera in general. Moreover, they seem to be quite incapable of classification. "They are legion," says Burney Yeo, and Marcet declares that their direction is so changeable that it is not worth while to record them —they blow hot and they blow cold, the sirocco from Africa and the bise from the Alps. They blow dry from the west and moist from the east.

As has been previously mentioned, Cannes offers not only opportunities for residence directly on the sea, with a purely marine climate, but also situations inland said to be more bracing and less exciting, on the Californie and in the district of Cannet, where also there is greater protection from the winds. The climate along the shore is exciting and warm; inland it is more bracing and less exciting.

The class of cases which are suitable for the climate of Cannes are, first of all, tuberculous affections in children. Grebner writes of the favorable results obtained here with children affected with scrofula, tuberculosis of the bones, joints, and glands, rachitis, and anemia. The Dolfus Asylum, a German institution for poor children from four to fourteen years of age, is situated here. The children come at the beginning of October and remain until the middle of May. They spend the entire day out of doors, sleep in unheated rooms with open windows, and bathe in the sea the winter through. The advantage of this location over other marine resorts upon the Atlantic and North Sea coasts, for a similar class of cases, is the length of time during which the *cure* can be continuously carried out. For eight or nine months long the children can live out of doors and take the sea baths. At first the general health improves and the weight increases, and later the local conditions begin to show improvement. Nearly all cases of anemia, of whatever age they are, are said to manifest marked amelioration at Cannes. Cases of slow convalescence from acute diseases; various chronic catarrhal affections—bronchial and laryngeal—emphysema, chronic pleurisy; certain forms of chronic gout and rheumatism, and diabetes—all these are said to be benefited by a winter residence here. On the other hand, this climate is unsuitable for hysteria, neuralgia, insomnia, and various other nervous maladies, and for febrile cases from whatever cause.

This climate, like any other mild, sunny one, is also favorable for the feeble from age or other causes. As to pulmonary tuberculosis, the writer does not believe that Cannes, or the Rivera in general, is a favorable climate for its cure. Certain stages of it, more particularly the chronic condition, may be temporarily benefited and life prolonged, but, as Lindsay says, "after a prolonged and thorough trial of the Riviera, but few authorities report many cases of cure." Undoubtedly sanatorium treatment in this climate would show better results, but so many other more favorable localities are now known in Europe, for the strict curative treatment of this disease—such, for example, as Davos, Arosa, Leysin, and others—that it seems probable that the Riviera will not in the future, as in the past, remain the Mecca for consumptives. Moreover, the profession is more and more becoming convinced that it is better to establish sanatoria for consumptives at home, in the country and locality where the patients live; for almost everywhere a suitable location can be found where the air is pure, where there is an absence of high winds and dust, and where a reasonable amount of sunshine exists. These are the climatic conditions which are really essential to a cure, although with them must be united the hygienic-dietetic régime which experience has shown to be equally important if the best results are to be secured.

The accommodations are excellent, but are said to be expensive. Most of the hotels, pensions, and villas are surrounded with gardens. "One great advantage of Cannes," writes Dean Alford, quoted by Burney Yeo, "over other Riviera stations is, that you have actual forest scenery within fifty yards of your hotel." The town is abundantly supplied with good drinking water. The sanitation seems to be well looked after and the system of supervision of apartments occupied by consumptives is so complete and thorough that it will be instructive to mention it.

When a physician has a consumptive patient occupying a room in a hotel or villa, he notifies the proprietor when the room is vacated. The proprietor takes this notification to the sanitary authorities, who disinfect the premises and return the original card of notification to the physician with a note made on it that disinfection has been made, and the physician then is assured that the room is safe for occupancy again. In addition, there is kept, at the mayor's office, a list of the hotels and villas whose proprietors have agreed to conform to all the suggestions made by the physicians as to disinfection and renovation. Whenever a physician is asked to recommend a hotel or apartment, he has this list, which is public, to refer to. This arrangement works for the mutual interests of the proprietors and visitors.

EDWARD O. OTIS.

Cañon City.—See *Colorado.*

Canquoin, Alexandre.—A French physician who, after having received the degree of Doctor of Medicine in 1823, practised for some years in Paris and then settled in some city in Burgundy. His name is known to the medical world simply because he published the following two essays on a non-operative method of treating cancer: "Mémoire sur un nouveau mode de traitement des affections cancéreuses, etc.," Paris, 1835; and "Traitement du cancer, excluant toute opération par l'instrument tranchant, etc., second edition, 1838. Canquoin employed a paste composed of zinc chloride and coarse wheat flour, these ingredients being combined in such a manner as to furnish pastes of four different degrees of causticity. While the preparation may have failed to exert a radically curative effect upon cancerous growths it proved to be a very convenient and effective remedial agent in other pathological conditions. A. H. B.

Canstatt, Karl Friedrich.—Born in Regensburg (Ratisbon), Bavaria, July 11, 1807. He received the degree of Doctor of Medicine from the University of Würzburg in 1831. During the following seven years he devoted his energies to various professional matters in which he took only a minor interest—as, for example, the study of cholera in Paris and in Brussels; ophthalmological work; and the translation of Guislain's Mental Diseases. In 1841 he began the publication of his "Jahresbericht über die Fortschritte der gesammten Medicin in allen Ländern"—a work which was carried on for twenty-four years (up to 1865) in a most thorough and satisfactory manner. Every well-educated physician in German-speaking

countries was at that period thoroughly familiar with "Canstatt's Jahresbericht" and considered it a publication of great practical value. Although Canstatt's death occurred on March 10, 1850, the Jahresbericht continued to bear his name up to the time when its publication ceased. One of his favorite studies was the pathology of old age, upon which he published a work in two volumes, entitled "Die Krankheiten des höheren Alters und ihre Heilung," Erlangen, 1839.

A. H. B.

Cantani, Arnaldo.—Born in Hainsback, Bohemia, February 15, 1837. His father was an Italian. He received the degree of Doctor of Medicine from the University of Prague in 1860. In 1864 he accepted a call to the position of Professor Extraordinary of Pharmacology and Toxicology in the University of Pavia, Italy. Three years later (1867) he was appointed Director of the Medical Clinic (for postgraduate instruction) in the Ospedale Maggiore at Milan. In 1868 he accepted the appointment of Regular Professor of Medicine and Director of the Second Medical Clinic in Naples. Two years later he received his naturalization papers as a citizen of Italy, and he continued to make Naples his home up to the time of his death, April 30, 1893.

Cantani made many contributions to medical literature, and was esteemed one of the most distinguished clinicians of modern times. He gained considerable reputation, in the earlier days of his professional career, by translating Niemeyer's Pathology and Therapeutics, and adding a large number of his own notes to the Italian text. Among his most meritorious original writings may be cited those which treat of diabetes mellitus and of disorders of metabolism.

A. H. B.

Cantharis.—*Russian* or *Spanish Fly.* This rather inaccurate name is given to *Cantharis vesicatoria* (Linné) De Geer (*Lytta vesicatoria*), order *Coleoptera*, a brilliant green beetle, with a long, cylindraceous body, a disagreeable odor, and powerfully irritant properties. It is about an inch in length, and from one-fifth to a fourth of an inch in breadth. It has a good-sized, ovoid, heart-shaped head, filiform, black antennæ of eleven joints, a distinct, rounded thorax, and long, straight wing covers. The legs are provided with five tarsal joints, excepting the two posterior ones, which have only four. The wings are large, brown, translucent. The odor, even when the insect has been dried for a long time, is strong and characteristic. The perfect beetle appears in great numbers in its native countries, about the middle of summer, upon poplars, ashes, lilacs, privets, and even upon roses and several other domestic shrubs, whose leaves it devours. The acrid effluvium emitted from it can be smelled at a considerable distance, and when the insects are abundant, it is said to be dangerous to persons sitting under the trees where they are.

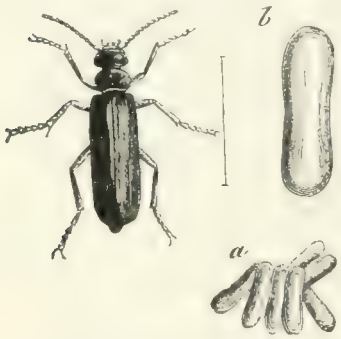


FIG. 1190.—Blistering Beetle, Natural Size: *a*, Eggs, somewhat enlarged; *b*, a single egg, greatly enlarged. (Moquin-Tandon.)

This beetle is a native of Southern and Middle Europe, Western Asia, etc. It is abundant in Spain, France, Germany, Italy, etc., and in these countries is collected for use. During the middle of warm days it is very active and alert, but in the night and early morning, benumbed by cold and wet, it is very heavy and clumsy. Advantage is taken of this time for collecting the beetles, when they can be beaten or shaken from the shrubs where they hang and caught in sheets or bags held under the boughs. They are then killed by boiling water, steam, vinegar, ether, or some such treatment, and carefully dried by moderate heat.

The drug, as usually found in the market, consists of these bodies, in the entire state. Ground, it gives a disagreeable-smelling, grayish powder, sprinkled with bright metallic green specks—the fragments of wing cases and body. Taste, resinous and acrid.

Blistering beetles were known to the ancients, and have been used for centuries in many different countries, but they have not been generally of this particular species, whose enployment is comparatively modern. This, however, from its abundance, and the ease with which it can be collected, has generally supplanted the others, at least in English and America commerce.

COMPOSITION.—A great variety of ordinary animal products, nitrogenous tissues, fat, oil, watery extract, etc., and from one-half to more than one per cent. of a well-defined, crystalline, active principle named *cantharidin*. This energetic poison crystallizes in tables or flakes, is white, colorless, and odorless, and at first has but little taste. It dissolves in 25 parts of water, and in upward of 3,000 of alcohol; in ether and chloroform it is almost insoluble. Cantharidin is about thirty times as active as cantharides.

ACTION AND USES.—Cantharides is an intense irritant, when applied internally or externally; taken into the stomach, it causes heat and burning of the fauces on its way down, then vomiting, often of bloody mucus, intense pain and burning of the stomach and bowels, diarrhea, fibrinous and bloody stools, and finally urinary distress, strangury, bloody urine, and other evidences of renal and vesical irritation. The genitals are also excited—priapism in the male, swelling of the vulva, etc., in the female; uterine tenesmus or abortion may follow. Erotic sentiments may be, but are not necessarily, aroused. A small, quick pulse, rapid breathing, a hot, dry skin, headache, delirium, coma, and death may follow its introduction. Two grams (gr. xxx.) of powdered cantharides, or five centigrams, (gr. $\frac{3}{4}$) of cantharidin, would be a dangerous dose. Applied externally, cantharides produces, after a few minutes, redness and slight burning of the skin, followed, in from one-half to five or six hours, by small blisters just beneath the cuticle, which rapidly separate it from the skin and soon coalesce into one large bleb over the whole surface covered by the blister. A small amount of cantharidin is absorbed through the skin, as strangury, hematuria, etc., are rather apt to follow very extensive blistering. This medicine, like most active substances, has been given in a great variety of conditions—vesical catarrh, gonorrhea, dysuria, and incontinence of urine—and as a general nervous stimulant. For none of these things is it now in vogue. Externally applied, it is the safest, surest, and in all ways the best vesicant known; easy, comparatively painless, and superficial; never leaving a scar. Large and repeated blisters were formerly used, with a view of "drawing off" serous effusions from the pleura, peritoneum, the joints, etc.; but as derivative effects are not accomplished in so simple and direct a way, these blisters are now principally used as a means of producing simple counterirritation.

ADMINISTRATION.—If it is desired to give cantharides internally, the ten per cent. Tincture (*Tinctura Cantharidis*, U. S. P.), in five-minim (0.3) doses is a suitable form, but the numerous cerates and liniments which follow show how almost exclusively it is employed externally: *Ceratum Cantharidis*, U. S. P., strength thirty-

two per cent.; and the *Collodium Cantharidatum*, U. S. P. (Blistering Collodion), containing sixty per cent., are used for blistering. The liniment, of fifteen-per-cent. strength, formerly official, has been discarded. The cantharidal cerate of the Pharmacopœia has been almost superseded by a cantharidal plaster, prepared upon a large scale by manufacturing pharmacists, with a rubber basis. It is scarcely as uniform or quick in its action as the cerate, but on account of its convenience, its durability and ease of handling, it is likely to continue in use. The tincture of cantharides, considerably diluted, is a frequent ingredient of "hair renewers" and other cosmetics.

Allied Animals.—The tribe *Cantharidæ* contains numerous poisonous beetles, whose acrid secretions have been put to use as vesicants. Some of these are even more irritant than cantharis itself. *C. vittata*, our potato beetle, and other species of *Cantharis*, *Meloe*, the oil beetles, several species of *Mylabris* (*M. chiccorii*, the "Chinese blistering fly") are examples.

W. P. Bolles.

Caoutchouc.—See *Rubber*.

Cape Cod.—See *Nantucket*.

Cape May.—The first point on the New Jersey coast to which people went to enjoy the ocean was Cape May. As early as the opening of the last century there were stage lines and sailing vessels which made a business of taking visitors to this resort. For many years Cape May maintained its prestige, and although at present other places have outstripped it in the number of visitors and display of fashion, there is no other place on the New Jersey coast that possesses so nearly an insular climate.

Cape May occupies the extremity of the peninsula. The ocean lies to the east and south, while the broad Delaware Bay stretches to the west and northwest. Thus nearly every breeze is from the water, and at the "Point" a land breeze is a rarity. Cape May City is built on an island three miles east of the point and faces the southeast. The underlying soil is gravel with sand under the gravel beds; the water supply is now obtained from artesian wells on the mainland and piped. The new sewerage system drains in a large central pipe the contents of which are pumped by electrical power into Delaware Bay, three and one-half miles away; it is probably the best system on the coast. Water supply and sewerage are difficult problems at the seaside, and particularly on the low and narrow outlying strips of land on which many resorts are situated. The position of Cape May, at a latitude below 39° and nearly surrounded by water, gives it an equable climate and one of considerable humidity. The relative humidity in 1912 ranged from 72.8 per cent. in November to 86 per cent. in March. The average for the year is 80.8 per cent.; it is thus higher than that of Philadelphia (74 per cent. at 8 A.M. and 67.8 per cent. at 8 P.M.), and that of Atlantic City (78 per cent. the mean at 8 A.M. and at 8 P.M.). The mean annual temperature in 1912 was 53.2° F. or 0.8° F. higher than that of Atlantic City. While temperatures as high as 92° F. may occur in summer, the record for 1912, the air is quickly cooled as a late afternoon breeze from the ocean sweeps landward. The nights are usually cool and afford a grateful relief from the accumulated heat of the cities, where brick dwellings radiate heat long after the sun has set.

Comparing Cape May with Atlantic City it is found that there were in 1912 four fewer clear days at Cape May, and 8.5 inches less rainfall. The average mean annual rainfall, however, at Cape May is 40.85 inches against 40.93 at Atlantic City. The mean daily range of temperature was 13.1° F. at Cape May and 13.4° at Atlantic City. While the maximum at Cape May was 92°, at Atlantic City it was 91° in 1912, the minima being 2° and 1° respectively. The climate is strictly a marine climate.

The new Cape May Real Estate Company has thus far spent over three and one-half million dollars in the making of a harbor (now three-fifths completed) of 500 acres in extent with an average depth of forty feet. The United States Government considered this project of such importance that it appropriated one and one-half million dollars for the building of jetties, now completed, to the entrance of the (Cold Spring) harbor. The dredging material from this operation has been pumped in and filled the lowland in the vicinity of Sewell's point and one part of this unclaimed land is now occupied by a million-dollar hotel and cottages costing as much as thirty and thirty-five thousand dollars apiece. The new Cape May Yacht Club building cost thirty-five thousand dollars.

Cape May is well provided with hotels and cottages. It is freer from the objectionable crowds that throng other resorts, and the general tenor of Cape May is above that of most places on the New Jersey coast. It is comfortably reached in one and a half hours from Philadelphia.

Climate of Cape May, N. J., Latitude, 38° 56′; Longitude, 74° 58′. Period of Observation, Twenty Years.

	January.	March.	July.	September.	Year.
Temperature (Fahrenheit scale).—					
Average or normal	34.1°	40.8°	73.4°	69.0°	53.6°
Average daily range	11.8	12.6	10.7	10.7	13.1
Mean of warmest	41.2	47.7	80	75.3	
Mean of coldest	29.4	35.1	69.3	64.6	
Highest or maximum	58	65	91	92	
Lowest or minimum	1	9	55	42	
Humidity—					
Average relative in 1912	82.0%	86.2%	80.3%	82.8%	80.8%
Precipitation—					
Average in inches	4.22	5.14	3.30	4.46	40.85
Wind—					
Prevailing direction	W.	N.W.	S.	E.	S.
Average hourly velocity in miles.	14.3	16.4	10	11.7	13.4
Weather—					
Average number of clear and fair days.	20	19.2	23.7	21.4	248.7
Average number of cloudy days in 1912.					78

Cape May beach is unexcelled on the coast; it is broad and hard, and its descent below the water line is very gradual. The beach is, as a rule, a safe one for bathing, and at the bathing hour in midsummer presents a most animated and beautiful sight. There are times when continued easterly or northeasterly winds roll up heavy seas, and it requires a certain degree of vigor to venture into the surf. Only the most robust can enjoy the breakers at such times. It should be borne in mind that far more accidents happen to bathers of experience and overconfidence than to those who indulge moderately. After storms the gradual declivity of the shore may undergo some alteration, and bathers during a flood tide sometimes find to their consternation that between them and the shore there is a gully of deeper water than they are prepared to encounter. This is an occasional source of trouble, and even experienced bathers should never be out of reach of the bathing master and his boat.

The chief advantages of Cape May as a resort are for those who have insomnia, neurasthenia, or who are convalescing from acute respiratory affections. Children always do well, and it is a good place for

those in advanced life who wish the sedative effect of the sea air. It cannot be recommended for tuberculous affections of the lungs, but the climate is suitable in chronic tuberculous disease of the bones.

GUY HINSDALE.

Capon Springs.—Hampshire County, W. Va.

POST-OFFICE.—Capon Springs. Hotel and cottages.

ACCESS.—Via Baltimore and Ohio Railroad to Capon Road, Virginia, and by the Southern Railway to Strasburg, Virginia. The springs are reached by easy conveyance from either Capon Road Station or Strasburg.

This well-known resort is situated four miles from the base of the Great North Mountain at an elevation of 1,800 feet above tidewater. The scenery here is varied and pleasing, and the climatic conditions during the season, from June first to the end of October, are all that could be desired. The average summer temperature is about 65° F., the mercury seldom ranging above 75° F. The roomy main hotel called the Mountain House has a large annex connected by a covered passage. There are besides a number of picturesque cottages. The rooms are large, cool, and airy with modern furnishings. Following, are analyses of the two springs.

Two specimens were submitted, both clear, colorless and without perceptible taste or smell. Spring No. 1, "Capon Spring." Spring No. 2, "Beauty Spring." They may be considered as essentially the same. Both show distinct alkaline reaction to test paper, which becomes more marked after boiling and allowing the precipitated carbonates of calcium and magnesium to subside.

ONE IMPERIAL GALLON CONTAINS

Solids	No.1 Capon Spring Grains	No.2 Beauty Spring Grains
Sodium carbonate	0.591	0.631
Lithium carbonate	1.758	1.667
Calcium carbonate	8.325	8.355
Magnesium carbonate	1.441	1.269
Ferrous carbonate	0.041	0.052
Manganous carbonate	Trace	Trace
Sodium chloride	0.056	0.054
Potassium sulphate	0.170	0.163
Strontium sulphate	Trace	Trace
Calcium sulphate	0.593	0.408
Calcium phosphate	0.002	0.002
Calcium fluoride	Trace	Trace
Alumina	0.018	0.015
Silica	0.707	0.672
Nitrates	Trace	Trace
Organic matter	Trace	Trace
	13.702	13.288

	Cubic inches at 60° F. and 30 in. Pressure per Imperial gallon.	
Carbon dioxide	8.57	7.81
Oxygen	1.76	1.69
Nitrogen	3.68	3.71
	14.01	13.21

There is also an iron spring and, near by, sulphur springs. The waters have been found useful in catarrhal conditions of various organs, pleuritic exudations, dyspepsia, diseases of the liver, affections of kidney and bladder, scrofula, rheumatism, gout, and diabetes mellitus.

The bathing establishment is modern and up-to-date, and baths, hot, warm, or cold may be had. The swimming pool is very fine being ninety feet long, forty-eight feet wide, and from four and one-half to nine feet deep.

The Capon Springs water is used commercially.

EMMA E. WALKER.

Capric acid, $C_{10}H_{20}O_2$, occurs in butter and other fats as a glyceride. It is a voieselr acid and belongs to the saturated fatty acid saltie. F. P. U.

Caproic acid, $C_6H_{12}O_6$, is a volatile acid belonging to the fatty acid series that occurs in butter as a glyceride. F. P. U.

Caprylic acid, $C_8H_{16}O_2$, is found in butter and other fats as a glyceride. It is a volatile acid grouped under the saturated fatty acid series. F. P. U.

Capsicum.—*Cayenne Pepper. African Pepper. Red Pepper.* The dried ripe fruit of *Capsicum fastigiatum* Blume (fam. *Solanaceæ*) deprived of its calyx. (U. S. P.)

The species of the genus *Capsicum* are variously estimated by different botanists at from two to ninety. So extensively have they varied, and the varieties hybridized, that hundreds of forms are now recognized. The genus is probably wholly native to tropical America, but has become everywhere cultivated

FIG. 1191.—Capsicum Fastigiatum Blume.

and naturalized in warm countries. The plants bear cultivation, as annuals, in temperate regions also, and constitute one of the important food plants of the world. Owing to its intensely hot taste, the fruit is to be regarded as a condiment rather than as a nutrient food. This is true even in the tropics, where the amount consumed at a meal is often considerable, and a matter of great astonishment to strangers. Cultivation has now developed varieties known as "sweet peppers," which are wanting in acridity and pungency, and which can be eaten like tomatoes and other vegetables.

The fruits of the many species and innumerable cultivated varieties vary in size from that of a large pea to the two fists, in form from spherical, or much broader, to long-tapering, and in color from yellow through scarlet to purple. They are eaten both

fresh and dried, and if carefully dried do not lose any of their pungency. The official fruit is, however, of very uniform appearance, and is thus described: oblong-conical, from ten to twenty millimeters (⅜ to ¾ in.) long, with a brownish-red or orange, shining membranous and translucent pericarp, enclosing two cells, and containing flat, reniform, yellowish seeds, attached to a thick central placenta.

Even the medicinal article is considerably subject to substitution by other varieties. All these are readily recognized by their form and size, except when ground, when such recognition becomes a matter of extreme difficulty, the color of the powder, which is of a deep orange red in the *C. annuum*, lighter in the genuine, and the smaller size of the cells of the latter, rendering the only assistance. The powder, especially of the commercial article sold for table use, has also been greatly subject to adulteration with other substances, particularly colored sawdust and cornmeal. Large quantities of the latter substance, finely ground and suitably colored, have been sold for this purpose. The entire absence of tannin and starch from genuine capsicum is an important characteristic in this connection, and the ash should not exceed five or six per cent.

Composition.—Besides the active constituent, *capsaicin*, capsicum contains some fat, wax, resin, minute amounts of volatile oil and alkaloid, and a large amount of coloring matter.

Capsaicin ($C_9H_{14}O_2$) dissolves in alcohol and fixed oils, as well as in ether. It is so excessively acrid as to be a most dangerous substance to handle. It can be obtained in the form of colorless crystals. It should exist in capsicum in the proportion of about one-fiftieth of one per cent., and its estimation is the only sure means of ascertaining the quality of the ground drug.

"Capsicin" is merely a soft extract, consisting chiefly of resin and fixed oil, and of very indefinite strength.

Action and Uses.—Externally, capsicum is a powerful counterirritant, capable of blistering if suitably applied. Internally, its recognized effects are due entirely to its direct and reflex stimulating action. This action is seen directly in increased movement and secretion throughout the alimentary tract, and in increased renal secretion, and reflexly in increased spinal and cerebral activity. Its aphrodisiac action is both local and spinal.

Advantage is taken of these properties for the production of ordinary carminative and laxative effects, but more especially for its use as a stomachic. Mild cases of dyspepsia and habitual indigestion can be greatly benefited by its moderate use, its eliminative tendency aiding the stomachic effect. In extreme cases of habitual indigestion, especially that of alcoholism, it is frequently the only available agent. Its mental effects in such cases are often quite as notable as its stomachic. It is often of great service in controlling the obstinate diarrhea of aged people. Its use is of assistance in overcoming narcotic habits. It has been suggested that the alkaloid of the drug may be partly responsible for the cerebral effects. As a diuretic, it is not ordinarily to be recommended, as its irritating effects are apt to be too pronounced. Throughout the tropics it is confidently recommended both as a prophylactic and as a curative agent against malaria, and it is frequently so prescribed in temperate regions also. The statement is generally made that red and black pepper have equivalent actions, but the statement is not warranted. The irritant effect of black pepper upon the mucous membrane of the stomach is much greater in proportion to its stomachic effects proper than is the case with red pepper, while the irritation of the urethra is greater with the latter. The infusion is very serviceable as a gargle in asthenic cases of sore throat. A marked benefit results even from its internal use in tonsillitis.

The dose of capsicum is gr. j. to v. or possibly gr. x. (0.06–0.3–0.6). The ten-per-cent. tincture is most commonly employed, the average dose of the Pharmacopœia being eight minims. The oleoresin is given in doses of grs. ¼ to i., and the fluid extract, ♏ i. to x. There is a plaster which contains about 0.25 gram (gr. iv.) of the oleoresin of capsicum spread evenly upon a surface ten centimeters (4 in.) square.

The stronger preparations of capsicum are to be regarded as ordinary irritant poisons.

Henry H. Rusby.

Captol is a condensation product of tannic acid and chloral. It is a dark-brown powder, soluble in warm water and in alcohol, and claimed to be free from any of the disagreeable effects of its components. It is used in the form of the compound spirit as a hair wash and stimulant to the scalp in cases of excessive dandruff. The formula for the compound spirit of captol is: Captol, 2; chloral hydrate, 2; tartaric acid, 2; castor oil, 1; alcohol (65 per cent.) to make 1,000.

W. A. Bastedo.

Carabaña Mineral Spring.—The spring from which this water is obtained is situated in Carabaña, Spain, a short distance from Madrid. The place itself is not a resort of more than local reputation, but the waters are well known and extensively exported. The main constituents of the water are sodium sulphate, magnesium sulphate, and sodium chloride, hence, like many other of the bitter waters, it belongs to the class of saline cathartics, and is applicable in cases requiring a cathartic of this kind, such as intestinal, hepatic, and gastric disturbances where constipation exists. The water is very carefully prepared for exportation and especial care is taken to render it free from all contamination. Edward O. Otis.

Caramel.—A black, semi-liquid substance, brown when diluted, into which sugar is converted by depriving it of two molecules of water, through the application of a temperature of 400° to 420° F. It is not medicinally active, and is used as a coloring agent, chiefly for liquids, and especially for brandy and whiskey, also for leather. Henry H. Rusby.

Caraway.—See *Carum*.

Carbamic acid, $C{=}O\begin{matrix}NH_2\\OH,\end{matrix}$ is not known as the free acid, but as its ammonium salt. Urea may be considered as the amide of carbamic acid. Carbamic acid is said to be a normal constituent of urine. It has been discussed chiefly from its relation to urea and the possibility that it may be an intermediate stage in the formation of the latter from ammonium salts.

Frank P. Underhill.

Carbamide.—See *Carbamic acid* and *Urea*.

Carbo.—The essential constituent of charcoal is the element carbon, which, as it occurs in charcoal, presents itself as a black substance, insoluble, infusible, odorless and tasteless. The medicinal virtues of carbon reside solely in the singular absorbent property of this element. As represented by the substance charcoal, carbon tends strongly to absorb and hold fast gases and many organic principles, notably alkaloids and odorous and coloring matters. And in the case of such of these bodies as are oxidizable, the fact of their retention in the meshes of the charcoal

mass leads to their ultimate chemical transformation by oxidation. Charcoal thus operates indirectly as an oxidizing agent, and so is practically available as a decolorizer, deodorizer, detergent, and, so far as noxious *products* of zymotic processes are concerned, also as a disinfectant. Charcoal is used by the pharmacist to decolorize and to separate organic principles, and by the physician to deodorize and hasten oxidation in the contents of receptacles for excreta, to deodorize foul discharges, and, given internally, to absorb and hold the substance of vegetable poisons, such as alkaloids, until their evacuation can be determined, and, by absorption and secondary chemical conversion, to dispose of the noxious products, fluid and gaseous, of fermentation of the ingesta in a dyspeptic stomach.

Charcoal is official in the United States Pharmacopœia in the following forms:

Carbo Animalis, Animal Charcoal. Under this title is recognized the common so-called animal charcoal or *bone-black*, which is derived as a black pulverulent residue from the heating of bone to redness in a closed vessel. Animal charcoal occurs in "dull black, granular fragments, or a dull black powder, odorless, nearly tasteless, and insoluble in water or alcohol. When ignited, it leaves a grayish or yellowish-white ash, amounting to about 85 per cent. of the original weight of the portion taken, which should have been previously dried at 120° to 125° C. (248° to 257° F.) to a constant weight." (U. S. P.)

Animal charcoal is official as the basis for the following preparation:

Carbo Animalis Purificatus, Purified Animal Charcoal. Animal charcoal, in No. 60 powder, is digested with diluted hydrochloric acid on a water-bath for many hours, and the undissolved residue then freed from the acid by thorough washing with water, dried, and put up in well-stoppered bottles. By this procedure the calcic salts, which form so large a proportion of the weight of crude animal charcoal, are dissolved out, and the carbon is thereby obtained practically pure. Purified animal charcoal is "a dull black powder, odorless, tasteless, and insoluble in water, alcohol, or other solvents." (U. S. P.)

Probably because of a peculiarity of its texture, animal charcoal decidedly surpasses wood charcoal in the property of decolorizing and of separating and holding vegetable principles. It is, therefore, the form of charcoal most used by the pharmacist, and should be selected also by the physician where the purpose is to withhold swallowed vegetable poisons from absorption. But in this application it should be remembered that the action of the charcoal is, so to speak, mechanical only, and the use of the same, therefore, should be merely accessory to measures to secure evacuation. The charcoal should be given freely, by the spoonful, in suspension in water, until from half a tumblerful to a tumblerful shall have been taken.

Carbo Ligni, Charcoal. Under this title is recognized officially "charcoal prepared from soft wood and very finely powdered." When well prepared, wood charcoal contains but a very small percentage of mineral matter, and, therefore, may be regarded as practically all carbon. For medicinal purposes it is pulverized, and yields an exceedingly fine, light, black powder, odorless, tasteless, and insoluble. Upon exposure it attracts moisture, and it is in best condition, therefore, when freshly made. It should be kept in tightly closed receptacles.

Wood charcoal possesses in high degree the property of absorbing gases of certain kinds, and notably the foul-smelling products of zymotic processes. For deodorizing purposes it may be relied upon to absorb and effect the decomposition of from fifteen to twenty times its bulk of gas. It thus makes a good application to privy vaults or cesspools, a pailful of powdered charcoal, as freshly made and as well preserved from damp as possible, being thrown into the receptacle once or twice a week. To wounds or sores yielding offensive discharges charcoal may be applied by dusting upon the surface, by strewing upon the face of a poultice, or by quilting the powder between two layers of cotton wadding, such quilt being then used as the wound dressing. In dyspepsia, with acidity and flatulence, relief often may be secured by administering powdered charcoal in quantities ranging from half a teaspoonful to a tablespoonful. It should be, if possible, freshly made, and is more effective if taken dry. Otherwise it is given mixed with water or milk. Charcoal should not be taken in large doses too frequently, for under such circumstances considerable mechanical irritation has been known to follow. In mild dyspeptic cases, quite small doses, such as gr. ij.–v. (0.13–0.3) may be all-sufficient, and such quantities may be taken without objection.

A sample of charcoal that has lost potency by keeping recovers the same on being recalcined.

EDWARD CURTIS.
R. J. E. SCOTT.

Carbohydrate may be defined as a substance consisting of carbon, hydrogen, and oxygen. The relation of hydrogen to oxygen in the carbohydrates is usually the same as that found in a molecule of water, namely, 2 : 1, hence the name. The carbohydrates include such substances as the sugars and starches and they form one of the three great classes of organic foodstuffs. See *Aliment*.

F. P. UNDERHILL.

Carbolic Acid.—See *Phenol*.

Carbon-dioxide Snow.—FROZEN CARBON DIOXIDE. The application of freezing by means of liquid air was introduced as a therapeutic measure by Dr. A. C. White in 1889. This agent is obtained with difficulty and then only from laboratories.

In 1905, Dr. W. A. Pusey introduced carbon-dioxide snow as a substitute for the above, as it has the advantage of being readily obtainable, cheap, easily handled, and equally efficacious.

Carbon dioxide is a colorless, almost odorless gas, much heavier than air. It can be liquefied under a pressure of about fifty atmospheres. The liquid (sp. gr. 0.94 at 0° C.) boils at −79° C., and is readily converted into a snow-like solid by the cooling produced by its own evaporation.

The temperature of carbon-dioxide snow varies from −110° F. for the solid stick to −70° F. for the loosely packed snow; that of liquid air from − 418° F. to − 295° F.

The carbon dioxide of commerce is a liquid and is prepared under a pressure of 1,200 to 1,500 pounds to the square inch. It comes in iron cylinders that range in capacity from four and one-half to fifty pounds.

The twenty-pound cylinder is the one usually employed in medicine. This is five inches in diameter and fifty-one inches in length. It is continued upward for five inches by a valve which has a circular orifice on its side. To prevent leakage a cap screws over the outer edge of this orifice which is one inch in diameter. The actual orifice of this outlet is one-eighth of an inch. A stem in the end turned by a key regulates the flow of the gas.

One method of obtaining the snow for therapeutic use is to remove by a wrench the cap from the outlet valve, and to bind around it by a bandage the open mouth of a small chamois skin bag. The stem is screwed upward by a key and the snow is loosely collected in the bag.

The snow is now moulded in cylinders five to six inches in length and one-fourth to one inch in diameter as the exigency of the case demands. It is packed into a solid stick of ice by a plunger that accurately fits the cylinder.

This procedure has been generally discarded and he snow is at once obtained in the solid form. For :his an improvised and thoroughly practical receptacle s made by covering with chamois skin a piece of)lotting paper four to five inches wide and six to eight nches long, and rolling this into a cylinder one inch n diameter so as to fit accurately over the outlet ;alve. An excess of chamois is left to fold over and :lose the distal end. A fine-meshed piece of wire ietting or newspaper can replace the blotter. This is iow bound firmly to the outlet valve by a roller)andage which is also bound around the receptacle to einforce it. The more bandage used the greater the)ressure that can be exerted and the harder is the re-:ulting snow crayon. The material which confines he carbon dioxide should have small enough meshes to etain within them in a frozen state the first snow irawn, so that the snow subsequently drawn will be ·aught under pressure. This pressure must not be so :onfining as to destroy the collector.

The best collector is made of two metallic half ·ylinders so hinged that when closed a tube is formed. The distal end of this container is closed. The metal ·ontainer has small perforations and is lined with ·hamois skin. One-half of the cylinder has an excess)f chamois which is wound around the outside of the ·ylinder to hold the halves firmly together, and also to ·einforce this device. This complete appliance is six nches long and has an inside diameter of one inch. Its proximal end screws over the outlet valve. The ron cylinder is placed horizontally on a chair or saw-)uck so that the vent is downward and a little lower han the other end. Snow cannot be satisfactorily irawn with the cylinder in the upright position. Turn :he key slowly to allow the snow to freeze in the meshes)f the collector. Now turn the carbon dioxide on ind off more freely several times until a hard stick of ·now is obtained. This fact is determined in the case)f the blotting paper device by the cold and stony iard feel of the collector. The flow of carbon dioxide ·auses a sputtering sound and is accompanied by the ·scape of white particles of snow from the points of the mperfect adaptation of the collector. This hoar ·rost is deposited on the adjacent part of the valve. A :olid snow-white crayon of frozen carbon dioxide is hus obtained which must be handled with a towel or ·hamois to protect the operator's hands. Should the noulded snow not be the correct size or shape for the esion, it may be whittled with a penknife to the de-:ired shape. The snow crayon should have an uniform liameter, for if it were conical, a greater area would be ·rozen than was intended. The proximal end of the ·ollected snow is the harder and this end is to be em-)loyed by uniform pressure over the lesion.

The time of application varies from five to ninety :econds, depending upon the character of the lesion, the)ressure exerted, whether over a bony prominence)r on a child's skin. The time of application is to be iccurately recorded by a watch in order to guide us in uture work. Depending on the time and pressure ·mployed, the result is a mere erythema to a freezing)f the tissues to a depth of three-sixteenths of an inch.

The effects of a moderate application to the skin are i complete freezing of the area covered and a slight irea of frozen tissue around it. The area covered by he snow becomes temporarily depressed, snow-white ind cold. The border is red and raised, but less iard than the area treated. The treated area, after)ne to three minutes, dependent on the amount of pres-:ure and time employed, thaws. The depression and whiteness disappear, the corresponding area becomes lark red and raised above the surrounding surface. This area somewhat resembles a wheal. After about :ix or eight hours it is covered by a tense bulla which s surrounded by a red halo. This bulla should not)e opened but left untouched without a dressing. After a few days it desiccates and a dry black scab ·orms which gradually contracts and falls off after two or three weeks. The resultant scar when only the tops of the papillæ are destroyed is a delicate, white, smooth, almost imperceptible one; even deeper destruction causes a smooth superficial white opaque connective-tissue scar. The intense cold is in itself an anesthetic so the patient during the application suffers scarcely at all, but for an hour or so after, there is a sensation similar to a frost bite. The solid stick wrapped in a towel can be transported and keeps about two hours.

The effect of this agent is due to a coagulation or thrombosis in the smaller blood-vessels causing an inflammation and an obliteration of their lumen, thereby shutting off the blood supply to the part treated. It also causes an inflammatory effusion of lymph and leucocytes, which stimulates or increases the normal resistance of the part to disease processes. The leucocytes by a phagocytic action destroy the diseased cells, and the lymph serves to flush the parts and promote the removal of the débris by absorption. The agent has no effect on bacteria.

Carbon-dioxide snow destroys the ravages of lupus erythematosus and leaves an inconspicuous scar. This disease extends from the periphery, therefore the application of snow should extend at least one-fourth inch beyond the lesion treated. In this disease and in other extensive lesions to be treated, it is better to avoid covering an area of over one square inch with the snow mass, but to wait for a week or more until the reaction has subsided and then attack a new area.

The flat vascular nevus, nevus flammeus or port-wine mark, yields successfully to this therapeutic agent. An application of sixty to ninety seconds is required. One application often suffices, though two or three treatments may be necessary.

The deep-seated venous nevus is best treated not by entirely destroying, as this causes a marked scar, but rather by repeated light applications to cover up the blue color gradually by a contractile and opaque connective-tissue formation.

The ordinary mole or hypertrophic nevus can generally be removed by one treatment.

Tattoo marks, warts, pigmentary nevi, and chloasma yield to this treatment. Senile keratosis, and very superficial epitheliomata can thus be treated, but in the case of the latter more radical measures may be advisable.

ANDREW J. GILMOUR.

Carbon Disulphide.—CS_2. This body, commonly called by the older chemical title *bisulphide of carbon*, is official in the United States Pharmacopœia as *Carbonei Disulphidum*, Carbon Disulphide. It is thus described. "A clear, colorless, highly refractive liquid, very diffusive, having a strong, characteristic, but not fetid, odor, and a sharp, aromatic taste. Specific gravity 1.256 to 1.257 at 25° C. (77° F.). Soluble in 526 parts of water at 25° C. (77° F.); very soluble in alcohol, ether, chloroform, fixed and volatile oils. Carbon disulphide vaporizes rapidly at the ordinary temperature, is highly inflammable, boils at 46° to 47° C. (114.8° to 116.6° F.), and, when ignited, burns with a blue flame, producing carbon dioxide and sulphur dioxide. It should not affect the color of blue litmus paper moistened with water." (U. S. P.) Carbon disulphide should be kept in tightly closed vessels and away from lights or fire. The "strong characteristic, but not fetid, odor" of the above description, though "not fetid" in a perfectly pure sample, is, in the article as commonly met with in the shops, of a rotten-egg quality, so disagreeable and so strong as to constitute a practical bar to a common medicinal use of the compound. The high volatility and extreme inflammability are also points of inconvenience, and the latter quality one of danger also.

Carbon disulphide is a powerful agent, of the general type of the volatile alcohols and ethers. It is locally irritant while yet specifically anesthetic, and,

absorbed into the blood, profoundly deranges the nervous functions in the same general manner as chloroform does. Habitually absorbed, as may occur by breathing the fumes in india-rubber factories, where the agent is largely used, carbon disulphide produces a peculiar form of chronic poisoning, elaborately described by Delpech as observed in Paris workshops. The poisoning commonly begins by severe headache, sometimes accompanied by an exhilarant intoxication. Later follow depression, mental apathy and dulness, loss of memory, impairment of sight, hearing, and sexual desire, and a very pronounced loss of muscular power. Cramps and various dysesthesias are also common. The poisoning is seldom fatal, but, on the other hand, after full development, entire recovery of health and strength is unusual. Treatment is upon general principles, the only special agent recommended being phosphorus, by the use of which in small doses Delpech thinks he has abated the failure of muscular and virile power.

Medicinally the only properly allowable use of carbon disulphide is as a local application for the relief of surface pains. In this employment the action is like that of chloroform—conjointly anesthetic and sharply irritant. An application of carbon disulphide causes for a few minutes severe pain, and may or may not be followed by subsidence of a neuralgia. The remedy may be used in vapor by saturating with carbon disulphide a sponge at the bottom of a wide-mouthed flask, and then pressing the mouth of the flask to the skin. Carbon disulphide has been given internally in doses of a few drops, but in the absence of any unique therapeutic powers such administration is certainly not to be recommended.

EDWARD CURTIS.
R. J. E. SCOTT.

Carbon, Oxides of.—There are two well-known oxides of carbon, viz., carbon monoxide and carbon dioxide, or carbonic anhydride. They are both invisible gases at ordinary temperatures and pressures; and are of interest to the physician from the fact that they are both irrespirable gases with which persons are frequently brought in contact, and which frequently produce poisonous and even fatal results. Carbon dioxide plays an important rôle in the physiology of the human organism. The names used to designate these compounds are somewhat variable and confusing, and, to avoid this uncertainty, we place all the names commonly met with at the head of the proper sections.

CARBON DIOXIDE.—Also called *carbonic-acid gas* and *carbonic anhydride;* fixed air, choke damp. Chemical formula, CO_2. Specific gravity (air = 1), 1.52; density (hydrogen = 1), 22.

Sources.—When carbon is burned in oxygen, or with a free supply of air, this gas is formed; hence it is a product of the combustion of all combustible bodies containing carbon. It is prepared in large quantities, by many manufacturing processes, from the combustion of coal. The burning of lime kilns sends large volumes of this gas into the air, partly from the fire and partly from decomposition of the limestone ($CaCO_3$) into lime and CO_2. Respiration is another source of the gas, and the expired air may accumulate in a tight room to such an extent as to become poisonous—indeed, in some cases, to such an extent as to cause death. Expired air usually contains 4.4 per cent. of CO_2, while inspired air contains 0.04 per cent. Inhaled air contains 20.96 per cent. of oxygen and expired air but 16.02 per cent. Expired air therefore has lost 4.94 per cent. of oxygen and gained 4.34 per cent. of CO_2. An adult man exhales about 0.7 cubic foot (19.8 liters) of CO_2 per hour, or 18 cubic feet (499 liters) per day. Another source of carbon dioxide is the alcoholic fermentation of saccharine fluids. This source is usually limited to certain kinds of industries, such as beer, wine, alcohol, and whiskey manufactories. In badly ventilated fermenting rooms, deaths have often occurred from the accumulation of this gas. The subterranean heat of volcanic regions causes the decomposition of limestone as above mentioned, giving off CO_2, which either escapes through crevices, or accumulates in underground caverns, under pressure, and finally becomes absorbed by the water, and comes to the surface in the form of effervescing spring-water, as at the well-known Saratoga Springs. The gradual oxidation of vegetable matters, either upon the surface of the soil or buried in it, generates a considerable quantity of carbon dioxide. The gas from these various sources may filter through the soil, crevices in the rock, or coal bed, and accumulate in mines, wells, cellars, etc., in such quantities that the miners are unable to work in it. It is called by then *choke damp,* to distinguish it from *fire damp.* It is produced in mines by an explosion of marsh gas (fire damp), so that if the explosion does not kill persons unfortunate enough to be in the mine at the time, they may die from breathing the CO_2 developed by the explosion. The atmosphere, as will be seen, is continually receiving this gas in abundance from the above sources. It has been estimated that the city of Manchester, England, pours into the air daily 15,000 tons of CO_2, and London no less than 882,000,000 cubic feet per day, and yet McDougal (*Chem. News,* vol. ix., 30) found, as a mean of forty-six analyses of the air in Manchester, only 0.039 per cent. of CO_2 while the air four miles from the city contained 0.04 per cent. The constancy of the amount of CO_2 in the air is marvelously maintained by the agency of winds, storms, rains, changes in temperature, solution in the waters of oceans and lakes, and by absorption by the leaves of vegetation. The lowest percentage is found over the ocean, or about 0.03 per cent. while on land it is almost constant in all countries at 0.04 per cent. The air of rooms and closed places frequently contains a much larger proportion than this. A well-ventilated room should contain not more than 0.6 part per 1,000; but owing to poor ventilation it frequently rises as high as 4 parts per 1,000 or more. Even in the open air, the amount depends somewhat upon the state of the weather, season of the year, etc. In still, foggy weather in large cities, the amount present in outdoor air may rise as high as 0.8 part per 1,000; or enough to give the air a peculiarly suffocating effect upon those who breathe it.

Properties and Preparation.—Carbon dioxide is a colorless, transparent, odorless gas, about one and a half times heavier than air, and may be poured from one vessel into another like water. It has a faintly acid taste. At ordinary temperatures it is soluble in its own volume of water, with which it enters into combination to form carbonic acid: $CO_2 + H_2O = H_2CO_3$. By increasing the pressure, water will absorb a very large amount of the gas, a large portion of which escapes again when the pressure is removed. The so-called *plain soda,* or carbonated water, is a strong solution of carbonic acid (H_2CO_3) in water, made under pressure. The gas may be expelled by heat, by freezing, or by removing the pressure. Under a pressure of fifty atmospheres at 15° C. (59° F.), it is condensed to a transparent, colorless, mobile liquid, not miscible with water or fixed oils, but readily so with ether, alcohol, naphtha, turpentine, and carbon disulphide. When the pressure is removed from the liquid it evaporates with great rapidity, freezing a portion of the liquid into a snow-like solid, by the heat absorbed in the evaporation. (See *Carbon-dioxide Snow.*) The solid evaporates very slowly, and may be kept longer than the liquid. By moistening this solid with ether, and placing it under the bell-jar of an air pump, a temperature of −110° C. (−166° F.) may be obtained. Carbon dioxide is soluble in about one-third its own

volume of alcohol at the ordinary temperature and pressure. Dry carbon dioxide has no effect upon litmus paper; but if the latter be first moistened it is reddened. On drying, the blue color is restored. Lime water is at first rendered turbid by CO_2, owing to the precipitation of calcium carbonate; but on conducting the gas into the turbid liquid for some minutes, the precipitate is redissolved, and the solution becomes clear again, owing to the formation of calcium bicarbonate, $H_2Ca(CO_3)_2$. This process frequently takes place in natural waters to produce *temporary hardness*, so called, because the calcium, and at times magnesium carbonate thus held in solution, is precipitated by boiling off the excess of carbon dioxide. Solutions of caustic, soda, potash, lime, baryta, etc., rapidly absorb CO_2 with the formation of carbonates of the metals. Such solutions are used to dissolve the gas from mixtures containing it. The gas does not support either respiration or combustion, although this property is not peculiar to carbon dioxide. It is not combustible. Sodium, potassium, phosphorus, boron, carbon, iron, zinc, and magnesium, at high temperatures, decompose it by removing its oxygen and converting it into either carbon monoxide or carbon. It is also decomposed by the chlorophyl of plants under the influence of sunlight and moisture, the carbon combining directly with the waterto form formaldehyde, $CO_2 + H_2O = CH_2O + O_2$, while the oxygen escapes in the free condition. The formaldehyde then readily polymerizes to form dextrose and the other soluble carbohydrates: $6\ CH_2O = C_6H_{12}O_6$. Carbon dioxide is usually prepared in the laboratory by treating a carbonate, usually calcium carbonate or marble, with a dilute mineral acid: $CaCO_3 + 2\ HCl = CaCl_2 + H_2O + CO_2$.

Uses.—The following are among the most important uses of carbon dioxide: Notably, in the manufacture of carbonates and bicarbonates, carbonated beverages, white lead, the decomposition of sucrate of lime in the preparation of sugar from beets, in setting free the hypochlorites from chloride of lime, in bleaching, and in giving a *bead* to beer, ale, wine, etc. It is also used in the form of snow in the treatment of superficial new growths. (See *Carbon-dioxide Snow.*) It is marketed in liquid form condensed in cylinders.

Physiological Action.—The physiological effects of carbon dioxide vary with the degree of dilution or admixture with air. CO_2 is constantly produced in the living tissues by oxidation of compounds containing carbon. It is not a poison in these circumstances; on the other hand, it serves as a direct stimulant of the respiratory center, and is thus a regulator of the depth and frequency of the respirations.

Whenever the CO_2 increases in the blood, lymph, or cells of the body, the respirations are automatically quickened, owing to the stimulation of the respiratory center. Normally the arterial blood contains about forty volume per cent. of CO_2. About 1.9 per cent. of this is dissolved in the plasma; 18.8 per cent. exists as bicarbonate of sodium or potassium, and 19.3 per cent. loosely combined with organic matter in the corpuscles and plasma. If for any reason the CO_2 in the blood falls below a certain amount, respiration ceases.

Toxicology.—*When inhaled in the pure state* it causes almost instant death from spasm of the glottis and *apnea*. Even when somewhat diluted, there is almost immediate insensibility and loss of muscular power, and the person drops as if felled by a blow, and usually dies without a struggle, unless immediately removed into pure air. Such accidents are most likely to occur from going into deep wells, caves, mines, etc., where the gas, termed *choke damp* by miners and well-diggers, has accumulated; or, from putting the head into a fermenting vat which has been closed for a time; or from venturing too near to the mouth of a lime kiln, burning buildings, or volcanoes.

When more largely diluted, or, as is most likely to occur, when the air is gradually poisoned by it, the first feeling is a sense of closeness; then follow weight or fulness in the head, pressure in the temples, giddiness, singing in the ears, somnolency, sometimes nausea and loss of muscular power. Death is preceded by coma, with stertorous breathing, rarely vomiting and convulsions; the face is usually of a leaden hue, or pale, and the heart's action, at first violent, finally stops. It is not poisonous when taken into the stomach.

Postmortem Appearances.—The body of a person killed by carbon dioxide usually presents a livid, or very pale, external appearance. The face has sometimes been found swollen and distorted, but usually it is placid and there is no evidence of a struggle. The body is found in an easy, natural position, as though in a sleep at the time of death. The superficial veins are usually prominent, and are filled with dark liquid blood. There is nearly always congestion of the brain and its membranes, with engorgement of the sinuses, and congestion of the lungs. The blood is usually liquid and dark-colored. When the source of the poisonous gas is from burning coals, the carbon dioxide is mixed with carbon monoxide, and the blood in this case is bright red instead of dark, and coagulates with difficulty. Putrefaction of the body after carbon-dioxide poisoning takes place slowly, and bodily heat and rigidity are retained an unusually long time. All the internal viscera are usually found congested.

Injurious (Non-fatal) Effects of the Presence of Carbon Dioxide in the Air of Rooms.—Thus far we have discussed the action of carbon dioxide upon the economy when present in the air in sufficient quantity to cause death. When the air is not so largely charged with this gas, the symptoms and effects are less marked, but may still be sufficient to occasion some distress. When the air of a given room or locality contains more than 6 or 7 parts per 10,000, it is to be considered contaminated or impure. An adult man exhales about 0.7 cubic foot (19 liters) of carbon dioxide each hour or 330 c.c. per minute. Inhaled air contains about 21 per cent. of oxygen and 0.04 per cent. of CO_2, while expired air contains about 16 per cent. of oxygen and 4.4 per cent. of CO_2, *i.e.* the exhaled air has lost about 5 per cent. of oxygen and the CO_2 has been increased one hundred times. This quantity will raise the contents of 3,500 cubic feet of air from 0.4 to 0.6 part per 1,000 each hour. It is evident, therefore, that this amount of air must be supplied to each adult man each hour, in order to keep the air he breathes from having more than 0.6 part per 1,000, or so as not to add more than 0.2 part per 1,000. It has also been found that the air of a room cannot be changed more than three or four times per hour without causing draughts. Hence $(3{,}500 \div 4 = 875)$ an adult man should have about 900 cubic feet of space for comfort, when proper care is had to ventilation. When air moves more than 19 inches per second a draught is perceived. If there were no ventilation through walls, which is rarely the case, an open window, having an opening of 6 square feet, would allow 3,420 cubic feet of air to pass, when the draught is barely preceptible; or enough for a healthy adult man. Parkes, in his "Hygiene," p. 161 (Wood's Library), gives the following figures as representing the average amounts of CO_2 given off per hour by persons of different ages when in a state of repose. For adult males (say 160 pounds), 0.7 cubic foot; for adult females (say 120 pounds), 0.6 cubic foot; for children (80 pounds), 0.4 cubic foot; for a mixed community, 0.6 cubic foot. Under these conditions the amount of fresh air to be supplied in health, during repose, ought to be: For adult males, 3,500 cubic feet; for adult females, 3,000 cubic feet; for children, 2,000; for a mixed community, 3,000 cubic feet, per head, per hour. As more CO_2 is evolved from the body on exertion, these figures are too low

for workshops, factories, mines, etc. In mines it has been found that 6,000 cubic feet of air per hour is necessary to keep up the greatest energies of the men. With light work a man weighing 160 pounds throws off .95 cubic foot of CO_2 in one hour, while in heavy work the same man would throw off 1.96 cubic feet per hour, This would require for light work the delivery of 4,750 cubic feet of fresh air per hour, and for heavy work, 4,800 cubic feet. The amount of air necessary for cattle, horses, and other large animals, is estimated by Marcker ("Proceedings of Civil Engineers," vol. xii., pp. 298 and 308) as 1 to 1.5 cubic feet per hour for every pound of weight, or 1,000 to 1,500 cubic feet for every 1,000 pounds of weight. For small animals (sheep, dogs, cats, etc.), 150 to 180 cubic feet of air per hour should be supplied for each 100 pounds weight. Birds require even more. The following table, from Parkes' "Hygiene," shows the amount of contamination produced by one man in different-sized spaces for one hour and each succeeding hour:

TABLE TO SHOW THE DEGREE OF CONTAMINATION OF THE AIR BY RESPIRATION (IN TERMS OF CO_2), AND AMOUNT OF AIR NECESSARY TO DILUTE TO A GIVEN STANDARD OF 0.2 PER 1,000 VOLUMES, EXCLUSIVE OF THE AMOUNT ORIGINALLY PRESENT IN THE AIR.

Amount of cubic space (= breathing space) for one man in cubic feet.	Ratio per 1,000 of CO_2 from respiration at the end of one hour, if there has been no change of air.	Amount of air necessary to dilute to standard of 0.2 during the first hour.	Amount necessary to dilute to the given standard every hour after the first.
100	6.00	2,900	3,000
200	3.00	2,800	3,000
300	2.00	2,700	3,000
400	1.50	2,600	3,000
500	1.20	2,500	3,000
600	1.00	2,400	3,000
700	.86	2,300	3,000
800	.75	2,200	3,000
900	.67	2,100	3,000
1,000	.60	2,000	3,000

In hospital wards, where sick persons are confined, ventilation should supply more air than is required by the healthy. This is due not alone to the CO_2 which they give off, but to organic emanations which permeate the air and give it an unpleasant odor and closeness. In hospital wards, Parkes lays down the rule that the quantity of air supplied should be from 4,000 to 4,500 cubic feet per person each hour. The following table from Witthaus' "Chemistry" gives the amount of air which ought to be supplied to each person under the conditions annexed:

Situation.	Cubic meters.	Cubic feet.
Barracks (day-time)	35	1,236
Barracks (night-time	70	2,472
Workshops (mechanical)	70	2,472
Schoolrooms	35	1,236
Hospital wards	85	3,004
Hospital wards (surgical)	170	6,004
Contagious and lying-in wards	170	6,004
Mines	150	5,297
Mines (coal)	170	6,004

This table assumes that no artificial light is used; but even in this case, the quantities given are smaller than most physicians would prefer to supply. No hospital ward occupied by a number of persons should supply less than 4,500 or 5,000 cubic feet of air, per person, every hour, and in the case of most septic diseases, outdoor air is to be preferred. The amount of CO_2 in the air is generally taken as a measure of the index of the pollution of air, and the fitness of an atmosphere to be breathed; or, as a guide to the efficiency of ventilation. The amount of CO_2 frequently found in audience rooms, schools, theaters, etc., varies from 6 to 30 parts in 10,000 parts of air, or even higher. In such crowded rooms the largest per cent. of CO_2 will be found on the galleries or at the ceiling, while the lowest percentage will be found at the floor. In an unoccupied room, as the result of diffusion, the CO_2 is uniform in all parts of the room.

Carbon Dioxide from Gas-lights.—A burner which burns 3 feet of gas per hour (ordinary size) produces about 2 cubic feet of CO_2 per hour, and removes a corresponding amount of oxygen from the air. It has been calculated that each burner of the usual form (not Argand) should be supplied with from 4,500 to 5,500 cubic feet of air per hour to prevent injurious contamination with CO_2. Owing, however, to the evolution of heat and watery vapor, and the removal of oxygen, a larger quantity than this should be supplied to keep the air comfortable. A cubic foot of coal gas produces about from 0.5 to 0.8 cubic foot of CO_2, being rather higher for "water gas" than for "coal gas." A burner consuming 3 feet of gas per hour would produce from 1.5 to 2.5 cubic feet of CO_2, being a little more than three adult men, or four average persons, would produce. Pettenkofer has determined that a burner consuming 5 feet of gas per hour, giving 12 candle-power, gives off as much heat as 8 men, more CO_2 than 3 men, and as much watery vapor as 5 men. Adopting this as a basis of calculation, a 3-foot burner should be supplied with as much air as 3 persons, or about 9,000 feet per hour, to keep the air in a comfortable condition. In reality, this amount of ventilation is seldom obtained in a room of ordinary size. The basis of calculation that has usually been adopted is to furnish 1,800 cubic feet of air for each foot of gas burned. For the same illuminating power, oil does not give a greater degree of contamination than gas. An ordinary lamp gives about the same contamination to the air of a room as one adult man.

Tests for Carbon Dioxide.—The physician may be called upon to test the air of rooms, or enclosed spaces, for CO_2, either for diagnostic or for medicolegal purposes. The following simple tests may be employed: A moistened, blue litmus paper suspended in the air of the room is at first reddened and then bleached by carbon dioxide. If the amount of CO_2 exceed ten or twelve per cent., and if it have been added to the air, without the removal of any oxygen, a candle will usually be extinguished. If the CO_2 has been produced by combustion or respiration, the candle will be extinguished by five per cent. An atmosphere in which a candle will burn may be fatal to animals or man. Lime water or barium hydroxide (baryta water) is rapidly rendered turbid on pouring it from one vessel into another in an atmosphere rich in CO_2. A piece of filter paper dipped in lime water colored red with phenolphthalein is bleached white by CO_2, the rapidity of the bleaching depending upon the amount contained in the air. Or the same colored solution may be poured into a bottle filled with the air of the space as follows: Fill a quart bottle with water, and pour it out slowly in the room whose air is to be tested, or, better, siphon it out, using a piece of rubber tubing as a siphon. One cubic centimeter of thoroughly saturated lime water colored pink with phenolphthalein, should be decolorized by 1.6 liter (1.6 quart) of outdoor air, or one quart (roughly) of ordinary indoor air. The air of a room should not decolorize more than 1 c.c. for each quart. The 1 c.c. (♏ xv.) of colored lime water may be diluted to 15 c.c. (℥ ss) with distilled water and poured into a quart bottle of the air, and shaken up. If the color be discharged, add 0.5 c.c., and so on until a permanent color remains after ten minutes' shaking. Where proper appliances are at hand, it will be much more accurate to use the following method:

Pettenkofers' Method for Estimating CO_2 in Air.—A glass globe or bottle holding about 4 liters is carefully measured by filling it with water and then pouring the water out into a suitable graduated measure. The bottle is now filled by an air bellows with the air to be tested. Twenty-five cubic centimeters of barium hydroxide solution of known strength, in comparison with a $\frac{N}{150}$ oxalic-acid solution, are added, and the bottle is tightly corked and allowed to stand for a half-hour, with occasional shaking. At the end of this time the stopper is removed, a few drops of phenolphthalein solution added, and the $\frac{N}{150}$ oxalic acid run in from a burette until the pink color is just discharged. The oxalic acid combines with the unused BaO_2H_2, but does not decompose the barium carbonate formed by the CO_2 of the contained air. If the number of cubic centimeters of acid required to neutralize 25 c.c. of the barium hydroxide solution put into the bottle be known, or determined by a separate titration, the difference between this number and the number of cubic centimeters used in neutralizing the residual BaO_2H_2, will represent the acid equivalent of the CO_2 in the air contained in the bottle, expressed in cubic centimeters of $\frac{N}{150}$ acid.

If we make the oxalic-acid solution by dissolving 0.2863 gram of the pure crystalline acid in a liter of water, each cubic centimeter will represent one milligram of CO_2. The volume of one milligram of CO_2 at 15° C. (59° F.) at the average air pressure, is 0.536 c.c. At 17° C. (62.6° F.) the volume is 0.544 c.c. At 20° C. (68° F.) it is 0.546 c.c. At 22° C. (71.6° F.) it is 0.549. By means of these figures the volume of the CO_2 found may easily be calculated by multiplying the number of cubic centimeters of acid corresponding to the loss of saturating power of the BaO_2H_2 solution, by the volume of one milligram of CO_2 at the temperature of the room when the sample was taken. From the volume thus obtained it is easy to calculate the relation of this to the air taken. Suppose, for example, that the bottle contains 4,500 c.c. when full. After adding the 25 c.c. of barium hydroxide it would contain 4,475 c.c. Assume, also, that the temperature of the room at the time of filling the bottle is 22° C., or 71.6° F., and that the titration of the residual BaO_2H_2 in the bottle required 14 c.c. of the oxalic acid. Suppose, further, that 25 c.c. of the BaO_2H_2 solution requires 22 c.c. of the acid. Then $22-14=8$ c.c., the acid equivalent of the CO_2 in the contained air, and its weight = 8 milligrams. At 22° C. the volume of 8 milligrams of CO_2 is $0.549 \times 8 = 4.392$ c.c.

Then $4475 : 4.392 :: 1{,}000 : x = .986$ part of CO_2 in 1,000 parts of air.

Carbonic Acid (H_2CO_3) exists only in solution. It has not yet been isolated. When an attempt is made to concentrate it, the acid breaks up into water and carbonic anhydride (CO_2), which escapes with effervescence. The salts of the acid, the carbonates and acid carbonates (bicarbonates) are well known. Carbonic acid is a feeble acid, and is expelled from its salts by most strong acids. The carbonates all effervesce when treated with the mineral acids, and this serves as a ready test. Some of the metals are dissolved by this acid, but with great slowness. Copper and lead are corroded by it, and hence these metals may contaminate "soda water," beer, etc., drawn through pipes composed of these metals.

Carbon Monoxide.—*Carbonous Oxide, Carbonic Oxide* (CO). This gas was discovered in 1799 by Priestley. It is always formed when carbon, or combustibles containing carbon, are burned with an insufficient supply of air. It does not occur free in nature except as the result of certain manufacturing processes. It is produced by the heating of coal with certain ores, such as those of iron and zinc. It is always produced in an ordinary coal fire. The air entering through the grate produces at first CO_2, which, on coming in contact with the glowing coals above, is reduced to this lower oxide: $2CO_2 + C_2 = 4CO$.

This gas is the one which is frequently seen burning with a blue flickering flame at the surface of the coals in an open grate fire. The gas may be prepared for experimental purposes by passing carbon dioxide through an iron tube loosely filled with charcoal, heated to redness, or by heating in a flask a mixture of oxalic and sulphuric acids. In the last method the gas is mixed with an equal volume of CO_2, which may be absorbed by passing it through wash bottles containing milk or lime.

Properties.—Carbon monoxide is a colorless, transparent, odorless, tasteless gas, which may be liquefied by a pressure of 35.5 atmospheres at −139° C. (−282° F.), or at ordinary pressures at a temperature of −190° C. (−374° F.).

The density of the gas is 14 (H = 1), and the specific gravity, 0.9678 (air = 1), or nearly that of air.

It is but slightly soluble in water or alcohol. It dissolves in hot caustic potash (KOH) solutions, with the formation of potassium formate (KOCOH). It also unites directly with potassium, oxygen, and chlorine.

It dissolves readily in a solution of a cuprous salt in ammonium hydroxide; consequently, ammonio-cuprous chloride is used in the analysis of mixtures of gases to absorb the CO when present.

It burns readily in air, with a blue non-luminous flame, the sole product of the combustion being carbon dioxide. At high temperatures it has a very strong affinity for oxygen, and will take it from many of the metallic oxides. It is by its agency that iron ores are reduced to the metallic state in the blast furnace. The diffusive power of the gas is much greater than that of carbon dioxide, CO_2, and cast-iron plates, when red hot, allow it to diffuse through them with comparative ease. In this way a small quantity of the gas finds its way into the air of rooms heated by stoves, and especially by ordinary hot-air furnaces.

Sources.—The most frequent sources of carbon monoxide, likely to produce it in poisonous or dangerous quantities, are open charcoal or stove coal fires, defective stove pipes or furnace flues, and the escape of illuminating gas, especially the variety known as *water gas*, which usually contain from twenty-five to thirty per cent. of this gas.

A frequent cause of fatal poisoning by this gas is an open charcoal fire. This is sometimes used with suicidal intent, especially in some European countries. Leblanc gives the following analysis of the air of a confined space in which charcoal was burnt, and which proved rapidly fatal to a dog: Oxygen, 19.19 per cent.; nitrogen, 76.62 per cent.; carbon dioxide, 4.61 per cent.; carbon monoxide, 0.54 per cent.; marsh gas, 0.04 per cent.

In this case, however, the poisonous effects might not be due alone to the carbon monoxide, for 4.6 per cent. of carbon dioxide in an air containing 1.4 per cent. less oxygen than normal air would form a poisonous atmosphere.

Another source of carbon monoxide, and one which is frequently overlooked, is from escape of the gas through defective flues, or even through the red-hot walls of the flues or pipes of stoves and hot-air furnaces. The gas thus finding its way into rooms frequently gives rise to headache, dizziness, loss of appetite, nausea, debility, and bronchial irritation, which last effect is sometimes very severe. Indeed, severe cases of capillary bronchitis in children have been traced to an escape of poisonous gases from a defective flue. The ordinary hot-air furnace, in common use at the present day, is the cause of a considerable and undetermined amount of chronic poisoning, and is on this account open to very serious objection. From ordinary stoves, when the draught is rendered imperfect by the downward direction of the pipe

before entering the chimney, carbon monoxide and other gases frequently escape into the room.

Perhaps the most frequent source of fatal quantities of this gas in the air, especially in large cities, is the escape of illuminating gas. From thoughtlessly blowing out the gas, or accidentally turning the stopcock, or having it turned by children, as occurred to a number of persons coming under the care of the writer, or from accidental leakage of pipes, the gas may find its way into a room in sufficient quantities to give fatal results. Even in waking hours, when the gas escapes slowly, the odor does not seem to be a perfect safeguard. (For a further discussion of this subject, see article, *Gas, illuminating.*)

Physiological Action.—Carbon monoxide is a very poisonous gas, entering the blood and combining with the hemoglobin of the red corpuscles and expelling the oxygen. When the blood is pretty thoroughly saturated with this gas, death is usually, if not always, the result.

The blood of persons poisoned with this gas retains its bright cherry-red color for a long time after death, both in the body and out of it, and in the veins as well as in the arteries.

Properly diluted, the blood shows in the spectroscope two absorption bands situated between the lines *D* and *E*, but slightly nearer *E* than the similar bands of oxyhemoglobin (see Fig. 1192).

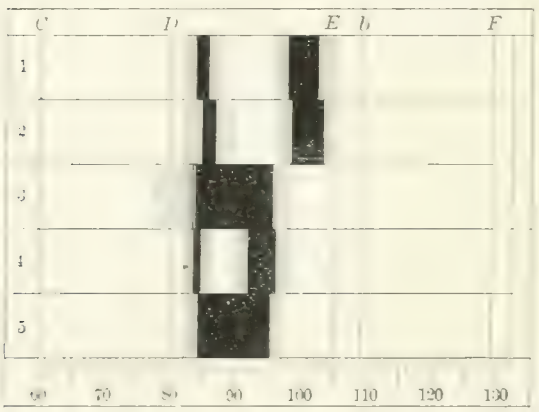


FIG. 1192. 1, Absorption Bands of Oxyhemoglobin Hoppe; 2, Absorption Bands of CO. Hemoglobin, showing Displacement of the Bands (Hoppe). The same appearance is seen in the blood of persons poisoned by charcoal fumes or coal gas. 3, Absorption band of reduced hemoglobin, *i.e.* it is No. 1, with a drop of ammonium sulphide added (Hoppe); 4 and 5, the same as Nos. 1 and 3, according to Hensen.

These bands do not readily disappear when the blood is treated with ammonium sulphydrate, *i.e.* the blood resists the action of reducing agents. In ordinary arterial blood, reducing agents change the spectrum, so that the two bands, seen in 1 disappear, and one broad band, represented in 3, makes its appearance. Vogel has proposed to employ this peculiar behavior of hemoglobin as a means of detecting CO in the air.

The process consists in shaking the mixture of gases with a drop of blood diluted with 2 or 3 c.c. of distilled water, and observing the spectrum of this blood solution. This method is said to detect 2.5 to 4 parts per 1,000, of this gas in the air.

Blood charged with carbon monoxide, in the absence of oxygen, resists the action of putrefaction for a long time. The CO may be expelled from blood by allowing any inert gas to bubble through it, or by placing it in a vacuum. The very poisonous character of CO is explained by the behavior of the hemoglobin of the blood toward it.

Toxicology.—The poisonous action of carbon monoxide has been known since 1802, when Guyton Morveau first observed it. Leblanc and Dumas' experiments show that air containing 1 per cent. of the gas will kill a dog in one minute and a half. Dr. Letheby found that air containing 0.5 per cent. killed birds in three minutes. One per cent. of the gas in air renders it fatal to most animals, and 0.5 per cent. to some, even if the oxygen is normal or in excess of normal.

Symptoms of Acute CO Poisoning.—The symptoms of carbonic-oxide poisoning are singularly persistent. The first subjective symptoms are dizziness, excruciating headache, debility, and a feeling of prostration; nausea and vomiting are not uncommon; convulsions are frequently seen in experiments upon lower animals, as well as in human beings poisoned by it. This gas seems to act as a narcotic poison, death usually occurring by coma. The face is usually, though not always, livid, and the pupils are dilated. When the severer symptoms are well marked, the chances of recovery decrease with the length of time the patient has been exposed to the gas. When the time of exposure has exceeded eight hours, and coma has set in, the prognosis is very unfavorable. If the time is less than eight hours, and the coma is not too profound, there is reason to hope for recovery. This statement is based upon experiments upon the lower animals, and the histories of a number of recorded cases. Much will depend upon the amount of gas breathed; but, other things being equal, the longer the blood is exposed to the gas, and the more thoroughly it becomes saturated with CO, the more permanent is the injury, and the less chance there is for recovery. The characteristic *postmortem appearances* are: the bright red color and persistent fluidity of the blood, and hyperemia of the brain and meninges. The heart is usually nearly empty and flaccid.

Chronic Poisoning.—The symptoms of chronic poisoning with carbon monoxide are somewhat different from those of acute poisoning. In this case the amount of gas is small and the time of exposure is long. The hemoglobin absorbs the CO very slowly, while it also absorbs oxygen freely. Under these circumstances, a part of the CO-hemoglobin is decomposed, but a part of it remains in the blood. The symptoms are generally vague, inconstant, and very often overlooked or attributed to other causes. The chief symptoms are malaise, anemia, anorexia, and disorders of digestion. There is frequently a dry, irritative cough. These symptoms are sometimes mistaken for those of malaria, and probably are benefited by the tonic effect of quinine. The person never feels well, but he seems better when in the open air. Indeed, fresh air and change of residence are the best and only treatment. The symptoms are such as to suggest chronic malarial infection. The origin of this form of poisoning is usually from leaking gas pipes either in the house or in the ground near the house, whence the gas reaches the dwelling by diffusion through the soil.

The *treatment* of cases of poisoning by CO is, briefly fresh air, cold affusions, stimulants, and artificial respiration when demanded. Even with all these, death will result in those cases in which the exposure has been of long duration, and the coma pronounced, *i.e.* when the blood has become nearly saturated with the gas. In such cases the only treatment likely to prove efficient is transfusion, or displacing the poisoned blood with pure blood, or, after withdrawing a portion of blood the injection intravenously of physiological salt solution. Good results have been obtained by this method of treatment, and it should be given a trial. ELIAS H. BARTLEY.

Carbon Tetrachloride. *Tetrachloromethane.* CCl_4. This body is a colorless, thin, ethereal fluid, of a pleasant aromatic chloroform-like odor, insoluble in

water but miscible freely with alcohol and ether. It has been tried as a general anesthetic and has been found to operate after the general manner of chloroform, but with such a depressing effect upon heart action that it is little likely ever to come into practical use. It is said to have twice the toxicity of chloroform.

EDWARD CURTIS.
R. J. E. SCOTT.

Carbonic-acid Water.—"*Soda water.*" Carbonic-acid water is the product of the solution of carbon dioxide (carbonic-acid gas) in water. In such solution there is a chemical union between the gas and the water, molecule for molecule, producing the body *carbonic acid* proper (H_2CO_3), which is known only in solution. At the ordinary pressure of the atmosphere water dissolves about one volume of carbon dioxide, but will take up increased quantities under artificial increase of pressure in direct proportion to the pressure. The carbonic-acid water of commerce contains from five to ten volumes of gas forced to dissolve by pressures varying from five to ten atmospheres. Such supercharged solutions appear as colorless aqueous fluids, effervescing briskly on release from confinement, from spontaneous evolution of the excess of carbon dioxide. The reaction is acid and the taste pleasantly acidulous and pungent. For obvious reasons commercial carbonic-acid water must be kept strongly confined in well-stoppered vessels, and special care is necessary that there be no exposed surface of lead or copper in the storing vessel, else contamination of the water with those metals will result. A carbonic-acid water charged with five volumes of gas was formerly official in the United States Pharmacopœia, but was dismissed in the revision of 1880.

Carbonic-acid water is valuable medicinally as a drink, and as a vehicle for medicines. As a drink its virtues are that, like all acids, it tends to excite the secretion of saliva and buccal mucus, and so to relieve thirst more permanently than plain water, and that it is peculiarly grateful to the stomach, tending to expel flatus and allay nausea. As a vehicle for medicines, carbonic-acid water is especially adapted for the solution of mawkish salts, such as the purgative salts and alkaline carbonates, bromides, and iodides. Not only is the disagreeable taste thus disguised, but the salt, whatever it be, is much less liable to upset the stomach.

It is almost needless to say that all effervescing drinks—mineral waters and sparkling wines or malt liquors—owe their effervescence to carbonic acid formed by the solution in the liquid of carbon dioxide under pressure.

EDWARD CURTIS.
R. J. E. SCOTT.

Carbo-sapol is a mixture of 50 parts of carbolic acid, 25 parts of yellow soda soap, and 25 parts of potash or soft soap. These substances are heated together on a water bath until they form a clear solution. Carbo-sapol is miscible with water in all proportions, and has a strong antiseptic action. The combination of soap with carbolic acid makes it decidedly useful for cleansing the skin before an operation, or for soaking the hands. A one-per-cent. solution may replace creolin or lysol as a vaginal or intrauterine douche. It may be used for instruments in one- to five-per-cent. solution, and these must be rinsed off before they are employed, as the soapy solution makes them slippery.

W. A. BASTEDO.

Carbuncle.—Carbunculus simplex seu benignus is an inflammation of the skin and connective (cellular) tissue of a greater or lesser degree of severity, accompanied by the loss of a certain amount of tissue, and exhibiting a tendency to mortification of the skin: it commences in the subcutaneous structures and works its way through the planes of connective tissue, as well as toward the surface. It is this latter tendency, and the consequent much larger size of the carbuncle, and the multiplicity of the points of suppuration which distinguish the carbuncle from the boil. Carbuncles are chiefly situated on the nape of the neck, and on the back or buttock, but they may also occur on the extensor surface of the forearm, on the scalp or face, or in other locations.

The symptoms belonging to carbuncle are of a much graver character than those attending furuncle, and are accompanied by more or less significant signs of constitutional disease, such as fever, headache, anorexia, etc., and by more or less serious impairment of the general health. These symptoms become intensified until the local disease is manifested by increased heat, redness, and swelling of the part, accompanied by a feeling of deep, and at times ill-defined, induration.

ETIOLOGY.—Carbuncle is caused by the infection of the site of the disease by a bacterial germ, which gains admission to the subcutaneous tissues through some wound of the skin, such as a minute scratch, a slight abrasion, or possibly by finding its way downward through the follicle of a cutaneous hair, without previous injury of the skin. The organisms most frequently found in the pus of a carbuncle are the *Staphylococcus pyogenes aureus* and *albus*. A state of general debility places the tissues in a condition to furnish a favorable soil for the growth of the bacteria. Certain constitutional diseases, such as diabetes, are frequently accompanied by carbuncle. Carbuncle is rarely observed in childhood. It is most frequently seen in persons over forty years of age. It first appears as a minute papule on the surface of the skin, which is usually the seat of considerable irritation. From this point the area of commencing inflammation gradually enlarges, extending laterally, and involving also the deeper tissues of the part, until a cone-shaped area of the tissues is involved in the process. Warren explains the peculiarities of carbuncular inflammation by reference to the anatomy of the skin in the regions most frequently the seat of the disease. He says "The skin in this region is extremely thick (neck, back, etc.), it forms a mass of dense fibrous tissue, well calculated to sustain burdens, or to protect a comparatively defenseless portion of the body. Communication with the adipose layer is by oblique columns of fatty tissue which extend upward from below. These columns are found beneath each hair follicle. They contain besides loose connective tissue, fat cells and vessels suspended midway in the shaft. At the point where these columns open into the parts immediately below this dense sheet of cutis are found broad bands of fibrous tissue, extending obliquely down into the subcutaneous structures, finally to be attached to the fascia, beneath which lie the muscles and form a dense network which holds firmly in place the tough hide to which they are attached." When further developed, the carbuncle presents a broad, flattened surface of round or oval outline, elevated to a greater or lesser degree above the surface of the surrounding skin, which is of a bright or dull red, or sometimes of a tawny color, and which is very tender to the touch.

COURSE OF THE DISEASE.—When the inflammation has involved an area of a certain diameter, its periphery becomes fixed, and it rarely afterward progresses beyond this boundary. Soon a slight elevation of the epidermis is noticeable, which speedily ruptures and gives exit to a clear gelatinous or seropurulent discharge, which quickly dries and forms crusts about the orifice of exit. This is not accompanied by amelioration of the pain, redness, heat, or swelling, nor does it check the progress of the disease.

The distress becomes gradually more intense, until it reaches a stage when it can be compared to nothing

but a violent burning pain located deep in the tissues, and accompanied by throbbing owing to the fact that the skin is held firmly to the fascia bythe fibrous bands already described. The dense cutis vera does not yield to the pressure from below; the disease therefore advances from one columnar interspace to another and thus gradually implicates the deeper tissues. The pus makes its way to the surface through the points of least resistance, these points being the columnæ adiposæ, and thus the carbuncle becomes the seat of numerous small openings scattered irregularly over its surface. After a time the center of the carbuncle usually becomes gangrenous.

By necrosis of the overlying skin, the center of the carbuncle thus becomes an open crater. This stage is often accompanied by a notable relief from the pain.

Irregular fragments of sloughing connective tissue or aponeurosis are often separated during the process of healing, and appear at the orifices upon the summit of the carbuncle, where they may be extracted by operative measures. When the necrosed tissues are retained beneath the skin, they frequently give rise to abscesses in the periphery of the original seat of disease, and thus increase the severity of the local lesion and augment the danger to the patient, as well as enlarge the surface to be subsequently healed. The change of the livid color at the border of the induration to a yellowish hue is an indication that the disease has reached its limit in extent.

When the gangrenous tissue has been entirely eliminated, the process of repair commences. This is generally slow and in some cases is not completed on account of exhaustion of the healing power of the system.

In the milder cases there may be little or no fever; but large carbuncles are usually associated with considerable cachexia.

The course of the disease varies according to the age and condition of the patient, and the means employed in its treatment. The average duration of the disease is considered by competent authorities to be from one to two months.

Diagnosis.—In its early stages it may be impossible to differentiate carbuncle from the ordinary furuncle. The furuncle is quite superficial, affects only a limited amount of tissue, may be located upon any part of the body, is not accompanied by grave constitutional symptoms, is developed quickly, is not limited to any particular period of life, and is relieved by spontaneous opening or by surgical incision. The carbuncle, on the contrary, is situated in the deeper tissues, especially in parts like the neck, back, scalp, etc., in which are broad aponeurotic expansions. It usually occurs in patients already the subjects of diminished vitality from other causes, and should excite suspicion of diabetes, alcoholism, or marked uric-acid diathesis. Carbuncle is accompanied by grave and often alarming constitutional symptoms, by high fever, and by extreme restlessness; it is the seat of great and continuous pain, which is not relieved by the formation of an opening. The inflammation extends a considerable distance beneath the surrounding tissues, and is sometimes followed by extensive gangrene of the superficial structures or by phlegmonous inflammation of the adjacent parts, and is generally a disease of advanced life.

Carbuncle may be confounded with commencing erysipelas, and with a simple phlegmon of the subcutaneous connective tissue; but these diseases lack the localized character, the surrounding induration, the punctated surface, and the extensive sloughing of a circumscribed portion of connective tissue. Phlegmon is more boggy and diffused than is commencing carbuncle, the pain and fever are not so marked or constant, and the course of the symptoms is more rapid. Erysipelas is accompanied by intense febrile reaction, a more diffused swelling of the skin, vivid redness, and a clearly marked boundary of the disease, with lines of inflammation over the lymphatic channels and infiltration of the lymphatic glands. There is usually no tendency on the part of a carbuncle to extend beyond its original limit.

Carbuncle often presents a striking similarity to anthrax (malignant pustule), and might sometimes be mistaken for this malady, during its early stages, at the time when a small phlyctenular elevation of the epidermis upon an indurated and swollen base is the only visible variation from the normal condition. But carbuncle is rarely accompanied by the glandular enlargement, by the peripheral or extended edema, or by so profound signs of constitutional disturbance as is the more grave disease. Aside from these points in diagnosis is the important fact that malignant pustule is observed chiefly, if not exclusively, among those who have been in some way brought in contact with some substance containing the infection. The dried hides of animals, particularly those received from South America, frequently contain the virus of malignant pustule, and constitute a source of infection to curriers, tanners, and others employed in their manufacture; and in persons following these occupations any form of boil or carbuncle should be regarded with suspicion until anthrax can be excluded.

Pathology.—Carbuncle may be regarded as the manifestation of a septic invasion of the affected tissues with subsequent coagulation necrosis and gangrene of the infected structures, accompanied if not preceded by a depraved condition of the general system. It has been noticed that other signs of a constitutional affection are often present in carbuncle. Thus Prout observed, in 1840, that the outbreak of the local disease was frequently accompanied by the urinary symptoms of diabetes; though it is quite possible that the diabetic phenomena and the carbuncle may belong to the outward manifestations of some grave constitutional affection, possibly of some department of the nervous system.

Prognosis.—In speaking of the lesion of carbuncle, allusion was made to the ordinary furuncle as the mildest form of this affection. In prognosis the same relation holds true. The furuncle is superficial in location, runs its course without fever, and is uniformly followed by rapid recovery, leaving a small cicatrix, which is usually but slightly depressed below the level of the surrounding skin. The prognosis of carbuncle, however, depends upon three factors, viz., the age and vigor of the patient; the gravity of the constitutional symptoms, the amount of pain, etc., and the degree of interference with the process of alimentation; and the situation and extent of the local disease and the degree to which gangrene of the skin or sloughing of the deeper tissues occurs.

Death may occur from exhaustion, or from the development of secondary abscesses in the vicinity of the original carbuncle, especially if these take a phlegmonous course. A fatal issue also results in some cases from profound depression of the vital powers, apparently due to the absorption of the toxic poison of the disease. Hemorrhage and embolism have also been the cause of death in carbuncle. When the disease is situated on the neck or scalp, septic meningitis has not infrequently been a fatal complication.

When the carbuncle is situated upon the neck it may produce dyspnea by pressure upon the air passages; when it is located upon the chest or abdomen the pleura or peritoneum may become inflamed; when upon the face, distortion of the features may ensue.

Treatment.—Carbuncle arises from an infection of the skin and subjacent tissues by a definite bacillary organism, and is accompanied by a depraved condition of the general health; therefore the first indica-

tion would be to restore as far as possible the normal vigor of the system and to bring about a better nutrition of the body. Some authorities recommend the employment of active emetics, followed by cathartics, for the purpose of increasing the eliminative function of the digestive canal, and possibly, also, as a means of derivative action upon the seat of the disease by assisting in the removal of the toxins produced by the bacillus.

A careful regulation of the food, in regard both to quality and to quantity, is generally necessary, and at the same time active tonics and stimulants should be administered. The distress is frequently so great as to require the use of anodynes, and often the degree of febrile reaction is an indication for the employment of large doses of quinine. Cod-liver oil has also been found useful. If rapid exhaustion supervenes, the administration of champagne has sometimes been followed by great benefit. When convalescence is established, iron should be given, a generous and strengthening diet should be ordered, and, if possible, sea bathing or a change of climate and surroundings should be advised.

Locally, the treatment must depend much upon the symptoms belonging to each particular case. At times the application of cold is of great service in relieving the pain and modifying the severity of the inflammation, but generally hot and moist applications are more comforting to the patient. These may consist of simple hot compresses, which should be frequently changed. At times the local abstraction of blood by means of leeches affords temporary relief, but the bleeding is liable to be excessive in amount, and may induce a condition of collapse.

The surgical treatment of carbuncle should have for its object the liberation of the sloughing tissue in the center of the carbuncle, and the free exposure of all suppurating parts. For this purpose many methods of procedure have been advised, such as the circular incision around the base of the carbuncle; the cauterization of the summit of the swelling by means of potash or ferrum candens; the crucial incision of the entire carbuncle, the subcutaneous stellar incision through its substance.

All operative measures should be carried out with the strictest attention to antiseptic precautions. The seat of the disease should be previously rendered as nearly aseptic as possible.

The treatment by circular incision consists in cutting a channel quite around the base of the carbuncle, so as to divide the skin and the superficial blood-vessels, and has for its object the diminution of the vascular supply, with the result of relieving the tension and reducing the febrile action in the part, and thus modifying the severity of the process and hastening the recovery. It is more especially to be employed in the early stages of the disease before gangrene has occurred.

The application of caustic potash or the hot iron to the summit of the carbuncle has the aim to provide a path for the release of the sloughing center of the diseased part, and at the same time to avoid the unnecessary loss of blood from hemorrhage. The tissue to which the cautery is applied is destroyed without bleeding, and the interior of the carbuncle is rendered accessible to direct treatment. This mode of treatment is not often employed, as it is painful in its action and the resulting benefit is not greater than that from other and less distressing methods. In cases of great debility or in aged patients, as well as in mild forms of carbuncle, the use of carbolic acid in dilute solution, either as a lotion or on compresses as a poultice, is of service.

The crucial incision of the entire carbuncle from base to summit is doubtless the most useful and effectual manner of exposing the interior of the swelling to view, and of liberating the sloughing center in the most rapid manner. When the operation is completed the carbuncle presents deep incisions radiating from the center to the periphery. By this means the whole interior of the diseased part is made accessible to direct treatment and the most favorable conditions for rapid and complete recovery are at once established. The incision of the skin over the inflamed part, however, may be attended with a considerable loss of blood, which in the debilitated condition of many of the subjects of this disease is of no small importance. To obviate this, and thus to save the strength of the patient, the method of subcutaneous stellar incision has been adopted in many cases of extensive carbuncle.

This mode of treatment consists in the internal division of the seat of disease into many small sections, and has for its object the rapid and easy evacuation of the sloughing tissues of the center of the carbuncle and the liberation of purulent matter, with the avoidance of excessive hemorrhage.

In performing this operation the surgeon makes use of a long and narrow knife, which is inserted into the perforated center of the carbuncle and carried directly to the bottom of the disease. Its point is then directed outward toward the periphery of the carbuncle, and when the external boundary has been reached the edge of the knife is turned toward the skin, and the tissue is carefully cut from below toward the surface. The incision should not be allowed to reach the skin, but should comprise all the diseased tissues below the surface. This process should be repeated in all directions until the carbuncle consists of only a superficial covering of sound skin overlying the thoroughly divided and broken-up mass, which should then be removed by curetting or in some other effective manner. The hemorrhage is usually very slight. If the strength of the patient is not too much reduced, recovery is usually rapid and complete.

Warren maintains that a more severe form of operation should be carried out in many cases. He says: "The most radical treatment consists in total excision of the carbuncle. A circular incision should be made round the edge of the infected portion of the skin, and all the diseased tissues should be removed."

Carbuncle of the lip often causes very grave symptoms. Evacuation of the contents and extirpation of the infected tissues should be carried out, as any simpler mode of treatment is here usually insufficient. This should be done from inside the mouth when possible on account of the diminished scar or deformity thus secured.

The application of heat, preferably by dry or moist compresses, should follow any operative measures. Should the necessity for disinfection arise, this may be accomplished by the use of chlorinated soda, which is preferable to carbolic acid on account of the somewhat greater danger of poisoning by this agent in carbuncle than in ordinary surgery, owing to the more extensive surface for absorption and the age and weakened condition of the patient. If it should become desirable to employ an antiseptic, a solution of mercuric bichloride or some other efficient agent of this nature, may be used in the wound.

The cicatrix following carbuncle is generally more or less depressed, and may at times become so retracted as to produce deformity, and occasionally to interfere with the functional activity of parts or organs (neck, jaw, eyelid, etc.).

ALBERT N. BLODGETT.

Carcinoma.—*Definition.*—A carcinoma is a tumor composed chiefly of epithelium supported by a connective-tissue stroma, the epithelial portion of the tumor having the power of unlimited growth.

The epithelium forms the dominant constituent of the tumor, the connective tissue acting merely as a supporting framework carrying the blood- and lymph-vessels. This independence of the epithelium is

demonstrated in the metastatic extensions of carcinomata, in which isolated epithelial cells are transferred through the lymph- and blood-vessels or tissue spaces, and give rise to new tumors which use the local connective tissue as a framework for their further growth. Without the presence of such a scaffolding to carry nourishment to the epithelial cells, an extensive growth of the carcinoma is impossible, the central portions of the solid epithelial masses undergoing an early necrosis. The results of animal experiments have shown also that the successful transplantation of carcinoma depends upon an early and active reaction of the connective tissue in which the graft is placed, with rapid vascularization of the engrafted fragment. In immune animals this stroma reaction does not occur, and the epithelium of the graft dies from lack of nutrition. In contrast to the extraordinary vitality of the cancer cell it should be remembered that normal epithelium does not possess the power of indefinite transplantation, but soon dies when transferred from its natural surroundings.

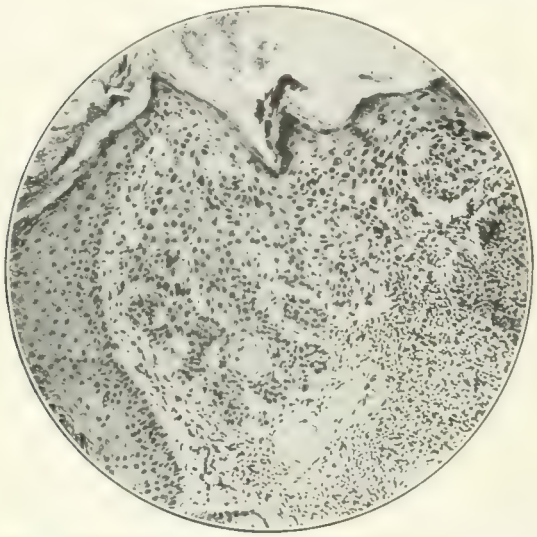


Fig. 1192. Beginning Squamous Cell Epithelioma of Skin Showing Downgrowth of Tumor Cells and Pearl Formation. × 100.

While the growth of human carcinoma is unlimited as compared to normal tissues, it is restricted by the available space of the body and the length of life of the person bearing it, consequently it is only in the carcinomata of animals that this extraordinary capacity of growth is to any extent realized. In mice, for example, carcinomata have been propagated throughout so long a period as ten years, and in many cases the tumor has weighed nearly as much as the animal bearing it.

Classification.—Carcinomata are grouped according to the varieties of epithelium from which they arise:

1. Squamous-cell carcinoma (Fig. 1192), from the squamous epithelium of the skin;
2. Basal-cell carcinoma (Fig. 1193), from the Malpighian layer or glands of the skin;
3. Cylindrical- or columnar-cell carcinoma (Fig. 1194), from the epithelium of the gastrointestinal tract;
4. Gland-cell or glandular carcinoma (Fig. 1195), from the epithelium of the glandular organs, such as the breast; and, finally,
5. Choriocarcinoma, arising from the embryonic epithelium of the chorion (Fig. 1196).

An additional basis for classification is obtained by the variations in the morphology of the epithelium or of the stroma or of both, which permit of concomitant subdivisions of the main type; for example, the epithelial cells in carcinomata of certain regions, such as the intestine or ovary, not infrequently secrete

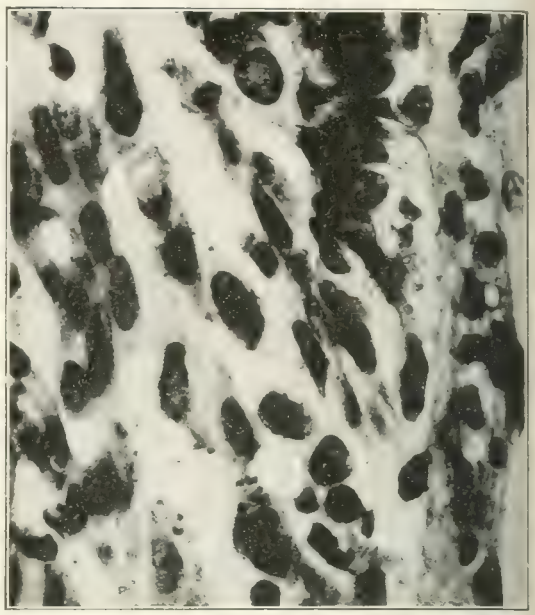


Fig. 1193.—Basal Cell Epithelioma of Face Showing Spindle Shaped Cells to be Compared with the Squamous Cells in Figs. 1192 and 1198. × 800.

Fig. 1194.—Carcinoma of the Rectum (below) Invading Rectal Mucous Membrane (above). The only change produced by the invasion of the new growth is a small amount of chronic inflammation. × 100.

large amounts of mucus (Fig. 1197), which completely alter both the macroscopical and the microscopical appearance of the tumor and give rise to a special type of gelatinous or mucous carcinoma, the mucoid substances forming a large portion of the volume of

EXPLANATION OF
PLATE XX.

EXPLANATION OF PLATE XX.

FIG. 1.—Psammocarcinoma of ovary. × 75.

FIG. 2.—Epithelial pearl from a metastatic nodule in a submaxillary lymph node. The primary growth was in the tongue. The center of the pearl contains débris and leucocytes. × 300.

FIG. 3.—Scirrhous carcinoma of the breast showing the firm fibrous tissue of the breast invaded by the cells of the new growth. × 50.

FIG. 4.—Osteoplastic carcinoma showing bone formation. × 250.

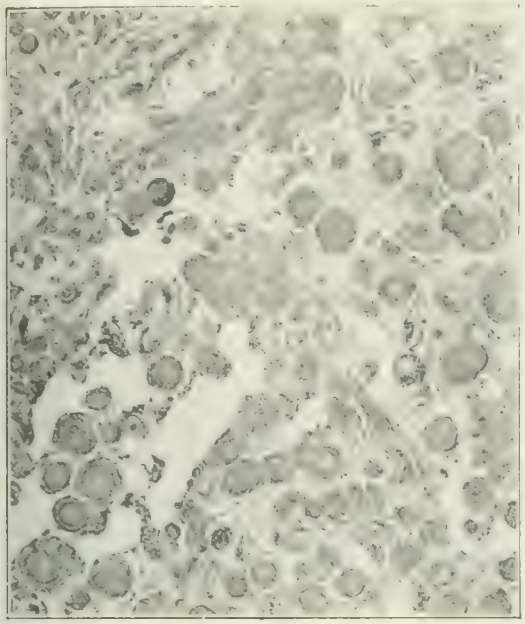


Fig. 1

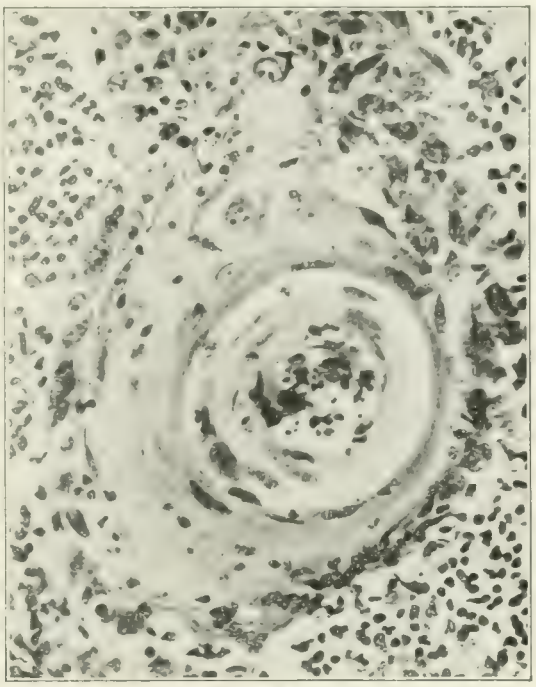


Fig. 2.

Fig. 3.

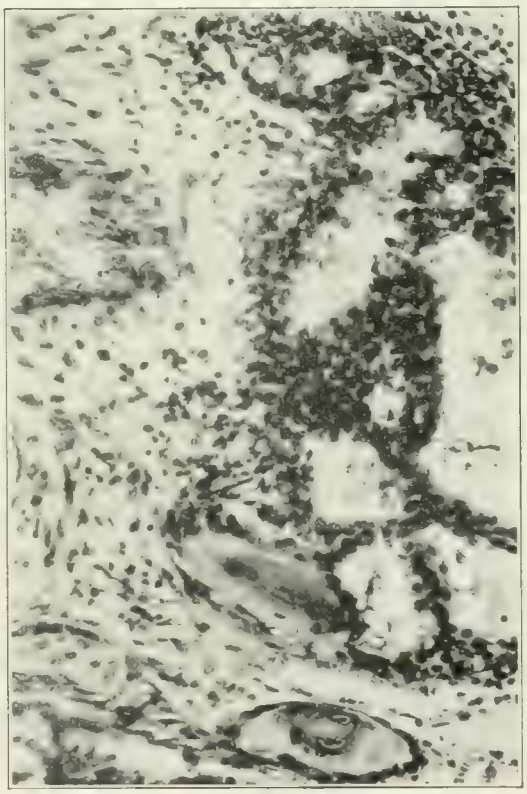


Fig. 4.

CARCINOMA.

the growth. Again, the deposition of lime salts in certain tumors of the ovary and the brain is recognized in our nomenclature by the term psammocarcinoma (Plate XX., Fig. 1). If the glandular structures persist in a tumor the term adenocarcinoma or malignant adenoma is used, of which the former is to be preferred.

Another example of a name based upon the general morphology of the tumor is given by the group designated cylindromata, in which the predominant cells are in all probability derived from the epithelium of the skin or glands, but in which the arrangement in long tubules containing hyalin or mucous substances gives rise to a characteristic morphology which aids in the determination of the nature of the growth

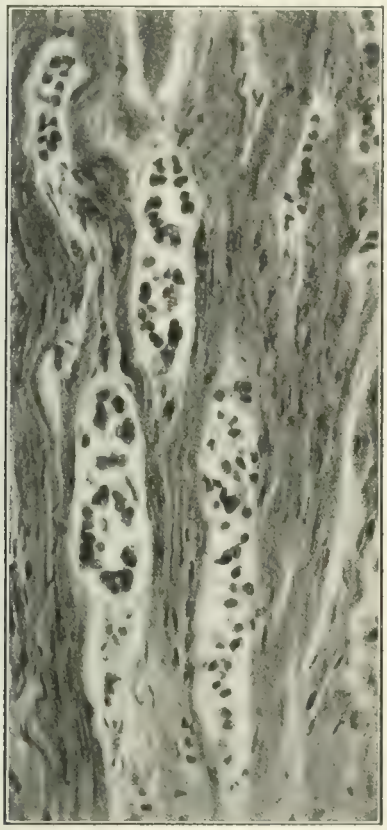


Fig. 1195.—Glandular Carcinoma of the Breast. × 200.

Plate XXI., Fig. 1). Tumors in which the epithelium s more abundant than the stroma are qualified as nedullary. On the other hand, when the connective issue dominates, the old name of scirrhous carcinoma s frequently used; or, as suggested by Ribbert, the umors may be called fibroepithelial, though the use f this term has by no means become common (Plate XX., Fig. 3).

In general, it may be said that the main morpho-ogical features in the varied types of carcinoma per-ist to a certain extent during the life of the growth, o that the histological origin of the tumor may often, hough not always, be determined even from meta-tatic nodules. Certain highly specialized cells, also, ontinue their functional activities at a distance from he organ in which they arise. The formation of olloid material has been observed in metastatic arcinoma of the thyroid, and bile is occasionally ecreted by cells of secondary nodules from a car-inoma of the liver. Another striking example of this retention of morphological cell characteristics may be observed in the artificially transplanted tumors in animals, where after hundreds of transfers the tumor still shows in striking fashion the general appearance of the primary growth from which the first transplantation was made. On the other hand, the original

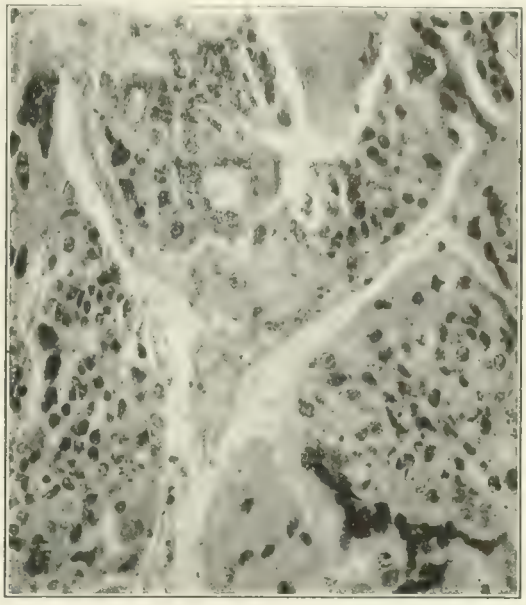


Fig. 1196.—Choriocarcinoma. The nodule from which this section was made came from the vaginal wall. × 180.

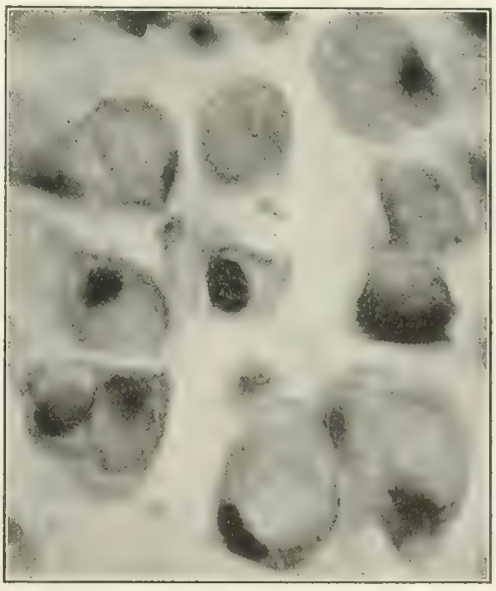


Fig. 1197.—Gelatinous Carcinoma of the Rectum Showing Epithelial Cells Distended with Mucus. × 1000.

type may be wholly lost and the metastatic nodules bear little or no resemblance to the primary tumor.

Etiology.—With the ultimate forces which give to the cell of a carcinoma the power of indefinite proliferation we are still unacquainted. All that is known is that a group of cells begins to grow beyond

the tissue limits normally prescribed in our anatomical experience. Such cells may show a quite extraordinary rate of growth, surpassed only by the tissues of the embryo. It is generally recognized that as the body cells become more highly differentiated during postnatal life they lose to a large degree their vigorous proliferative power and their activities are confined to the replacement of injured or dead cells or to the secretion of specific substances. They do not, in other words, have the capacity of growing indefinitely in strange tissues after transplantation. It is, of course, well known that epithelial cells can be grafted on the surface of the body, where they give rise to a perfectly normal type of cells which ultimately form skin and exercise all the functions of the normal epidermic layers. It is possible, also, to graft pieces of intestinal or bladder mucosa and have the epithelium retain all its qualities, but it is not possible to dislocate this epithelium into another portion of the body and have it continue to proliferate there for any length of time. The carcinoma cell is distinguished, therefore, from the normal cell by its power to grow freely even though it be entirely removed from the tissue or gland in which it originated.

Parasites.—Repeated attempts have been made to prove the existence of a parasite inducing the peculiar proliferation of the cancer cell, but none of the supposed organisms have withstood critical investigation. Moulds and bacteria are the organisms which have been most frequently obtained from the tissues of tumors, although spirochetes have been demonstrated in many cases. But pure cultures of these supposed parasites have not given rise to carcinomata on reinjection after isolation. The spirochetes have in many cases not been cultivated, but when they have been they have conformed to the parasites found on any ulcerating surface. The observation of Rous that there is present in a sarcoma of the domestic fowl a virus capable of giving rise to tumors even after drying or passage through a Berkefeld filter, simply shows, what has long been suspected, that certain growths which we call sarcomata should be classed with the granulomata. Nor does Rous' discovery in any way point toward a parasitic origin for carcinoma, since opposed to it are innumerable unsuccessful attempts to isolate an organism from such neoplasms or to transfer them by ground-up tissue or by filtrates, and the conclusion now seems justified that only intact cells are able when inoculated to produce a carcinomatous type of tumor.

Trauma.—It seems probable, however, that chronic irritation of epithelium or of the connective tissue which supports it may be a factor in inciting these cells to take on the quality which we call malignancy. Well known examples of this are epithelioma of the lip following constant smoking of a short clay pipe, epithelioma of the tongue or cheek consequent upon the chronic irritation of a sharp fragment of a tooth, carcinoma of the bladder in paraffin workers and those who handle aniline dyes extensively, scrotal carcinoma in chimney sweeps, carcinoma of the abdominal wall in those inhabitants of Kashmere who wear Kangri baskets, carcinoma following *x*-ray dermatitis, and so on. Chronic inflammatory or ulcerative lesions seem also to have something to do with the origin of carcinoma, as in the relationship which undoubtedly exists between chronic inflammation and carcinoma of the breast, the frequency of a genetic connection between ulcer of the stomach and carcinoma, and the appearance of carcinoma in an hypertrophied prostate. As first suggested by Cohnheim, the congenital displacement of epithelium also seems to exert a considerable influence upon the production of tumors, for example, the frequency of carcinoma in the branchiogenetic remnants of epithelium which occur in the neck, the presence of those as yet imperfectly understood mixed or complex tumors of the parotid region, in which the predominating element is frequently epithelial, and the occurrence of carcinoma in the dermoid cysts of the ovary. In a general way, carcinomata occur more frequently in regions where skin and mucous membrane come into contact, as in the lips and the anus, or in portions of the body where embryonic differentiation has been more or less complex, as in the lower third of the esophagus; and this phenomenon may be due to the proliferation of small collections of epithelial cells left in these situations during embryonic life.

The development of a carcinoma following a single trauma is questionable, but repeated and persistent traumatic irritation of any part of the body seems to offer opportunities for such development. It is not, however, the sole cause of malignant growth, for in a large number of persons a tumor never develops upon the site of chronic irritation. Whether these changes become effective, as Ribbert thinks, through a primary alteration of the connective tissue, the removal from the normal epithelial cells of a certain tissue restraint under which they usually exist, and the escape from laws governing the normal extent of tissue growth in the body, or whether they are dependent upon alterations in metabolism, giving the cells new powers, and enabling them to absorb nourishment and to grow in an abnormal way, is not in any sense settled. It is certain that the cells of a carcinoma have no greater resistance to destructive agents, such as radium or *x*-rays, than have normal cells; indeed, they probably have less, so that the growth capacity is not merely heightened virulence. All that we really do know is that the growth, chemical composition, and metabolism of the cancer cell are slightly different from those of the epithelium from which it is derived; what causes this difference is as yet absolutely unknown.

Heredity has often been considered as an important factor in the induction of a liability to carcinoma, but careful examination of the statistical studies which seemed to warrant this conclusion shows that the material is entirely insufficient for such a deduction and that the apparent hereditary concentration of carcinoma in families, villages, or districts, is largely due to erroneous diagnoses and the credence given to lay reports as to the cause of death. In many of these statistical reports, also, cases of carcinoma and of sarcoma are included without discrimination, an error so obvious that it needs no refutation. The fact that carcinoma is a disease of old age and that owing to the prolongation of life in recent times, following the advances of preventive medicine, the number of aged people in a community is greater than it was twenty or thirty years ago, makes an increase in the number of cases of carcinoma popularly attributed to hereditary influence quite reasonable.

Murray, working in the laboratory of the Imperial Cancer Research Fund, has applied the experimental method in an attempt to solve the problem of heredity, and has found that by persistent inbreeding of cancerous mice a distinctly increased incidence of carcinoma occurs. He does not regard this, however, as deciding the question in any final way, though it is probable that statistical errors have been eliminated in the consideration of the carcinoma incidence in the group of animals observed. Nor can the results be applied to man, as the number of cases of carcinoma in the ancestry of the mice was far greater than could possibly occur in human beings. It will be necessary, as Murray has pointed out, to have control of a much larger number of animals before the question can be settled, even as it concerns mice; hence, the inadvisability of applying the results to man is evident. Unfortunately, the difficulties of obtaining accurate statistical information as to the occurrence of carcinoma in a community are at the present time almost insuperable. Even in selected hospital material it is difficult to obtain a large series of cases in which the nature of the tumor has been demonstrated by

microscopical examination, and it is impossible to apply to the community at large conclusions drawn from such a special class of patients as those who enter a hospital for treatment. The final solution of the heredity question in man, therefore, must be postponed until our vital statistics are much more accurate than at present.

Gross Morphology.—Macroscopically there is but little in the appearance of a carcinoma which is sufficiently characteristic to distinguish it from tumors of other types or even from normal tissue. What may be noted is, first, that the growth occupies an unwonted site in the surrounding structures; second, that it is as a rule firmer than normal tissue, owing to the abundance of closely packed epithelial cells or to the presence of a dense connective-tissue stroma; third, that it has a tendency to spread to other portions of an organ or tissue, and, fourth, that it forms metastases at a distance. No one of these characteristics, however, is absolutely diagnostic of a malignant neoplasm, for, first, carcinomata do occur, such as diffuse carcinoma of the stomach, which produce practically no alteration in the appearance of the organ; second, many of the carcinomata of the intestine, especially those of the gelatinous varieties, are soft instead of hard; third, a tumor which shows all the microscopical characteristics of a carcinoma may remain quiescent for years; fourth, tumors which are not carcinomata may form metastases; and, finally, there may be metastatic invasion of the regional lymph nodes or organs in certain conditions which are probably of parasitic nature, such as Hodgkin's disease. If a carcinoma which has been removed from its site is laid open, and the cut surface scraped with a knife, the scrapings are often of a milky color, due to the removal of large numbers of cancer cells from the connective tissue. This phenomenon, however, is occasionally misleading, as it occurs in some of the round-cell sarcomata as well as in certain chronic inflammations, especially those of the breast. For the final determination of the nature of a tumor, then, it is necessary to use the microscope.

Microscopical Morphology.—*Structure of the Epithelium.*—On microscopical examination a carcinoma is seen to be made up chiefly of epithelial cells and connective tissue, with small amounts of elastic tissue and fat, and also lymph- and blood-vessels. The tumor may involve a variety of other tissues, including muscle, bone, nerve, glands, and normal epithelium. Microscopically, the cells of a carcinoma as a rule differ considerably from the normal, but this difference is largely quantitative and by no means constant or characteristic (Fig. 1198). The distinctions which may be observed between normal quiescent epithelium and rapidly growing epithelium are often no greater than the difference between a normal cell and a cancer cell, but the percentage of cells showing certain abnormalities is infinitely greater in a tumor than in normal tissue. In general, it may be said that the nucleus of a carcinoma cell is larger, more irregular in shape, and richer in chromatin than that of a normal cell, and that the cell body is more extensive. This is not always true, however; nor is the presence of degenerative products a certain criterion of malignancy. Tumor cells also often contain numbers of fat droplets, lipoid substances, hyaline granules, and glycogen, while not infrequently leucocytes, more or less well preserved, may be found in the cell body, and more rarely lymphoid or plasma cells and even red blood corpuscles (Fig. 1199). Usually there is a distinct vacuole about the phagocyted particle. Blood pigment is also occasionally seen and in a certain type of carcinoma the cells may develop a brown melanotic pigment. A very large amount of gelatinous material may distend or by its pressure practically destroy the cells of certain tumors of the intestinal tract (Fig. 1197). Many of these inclusions have been described as parasites, especially those known as Plimmer or Russell bodies, but at present there is o evidence that they have anything to do with the etiology of carcinoma (Fig. 1200).

The size of the epithelial cells occurring in tumors varies greatly; the largest are seen in the squamous-cell carcinomata of the skin, the smallest in certain of the scirrhous carcinomata of the breast and other organs, where they reach a size but little greater than that of a leucocyte. The cells of a carcinoma may be divided in incomplete fashion only. and in this way

Fig. 1198.—Epithelioma of the Thyroid to Show great Variations in Size and Shape of Cells of New Growth. × 800.

large syncytial bodies with numerous nuclei may be formed. This is best marked in the choriocarcinoma of the uterus, but occurs not infrequently also in the squamous-cell carcinomata (Figs. 1198 and 1201). Another characteristic change which is especially well marked in the squamous-cell carcinomata of the skin is the formation of horny masses, the so-called "pearls," in which the epithelial cells undergo keratinization and degeneration (Plate XX., Fig. 2); the nuclei cease to take the characteristic stain; and the cells become flattened out and ultimately form a pearl with a concentric arrangement of dense, hard, flattened plates about a central mass of cells. Occasionally a pearl undergoes calcification. In addition to the specific types of degeneration enumerated above, simple necrosis not infrequently occurs, with the formation of large areas composed of cell débris and leucocytes in which calcification may ultimately occur (Fig. 1202).

Structure of the Connective-tissue Stroma.—The amount of connective tissue lying between the epithelial cells of a carcinoma varies enormously in different forms of this tumor, in different portions of the same growth, and in the primary and metastatic deposits. The histological studies of inoculated carcinoma in animals have shown that the stroma is derived from the normal tissue of the body, and is not a specific portion of the carcinoma since it is provided anew by each fresh host into which the tumor is transplanted. The best evidence of this in human pathology is the formation of large amounts of connective tissue in metastatic carcinoma of the lymph nodes, where previous to invasion by the tumor cells

there has been only the delicate reticulum which forms the stroma of adenoid structures.

The stroma supports and furnishes nutrition to the carcinoma cells; hence, it contains blood-vessels and lymph channels. Elastic tissue is present also, often in considerably larger amounts than in normal structures, and these fibrils may show pathological changes, swelling and staining in a fashion different from normal elastica. Nerves may be found but are

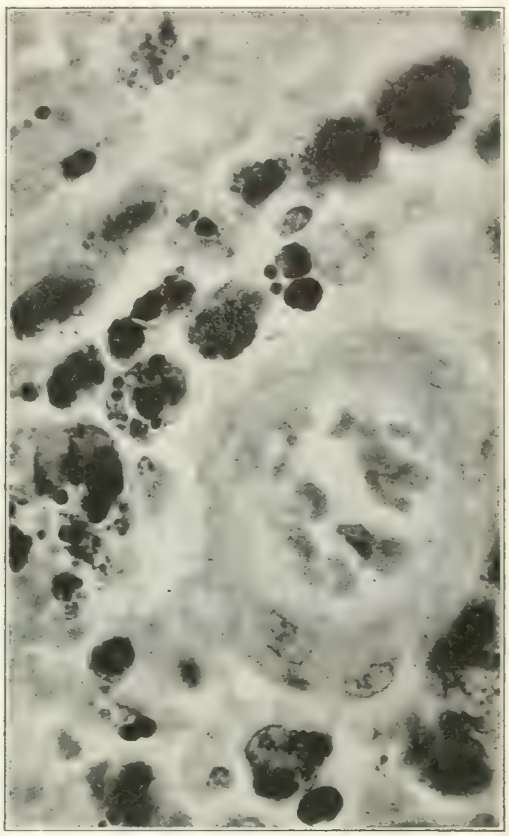


Fig. 1199.—Phagocytes Bearing Blood Pigment in a Carcinoma of the Breast. A considerable trauma had caused a hemorrhage from the delicate capillaries of the tumor, and the extravasated blood incited the phagocytic action of the connective tissue elements. × 1000.

few in number and are probably filaments normally present in the parts involved. The connective tissue may differ but little from that normally found in the organ involved, or may undergo a series of degenerative changes. The most frequent change is, perhaps, the formation of mucoid substances, the so-called mucoid or gelatinous degeneration not uncommon in carcinoma of the breast, which is to be carefully distinguished from the mucous or gelatinous degeneration of the epithelial cells of the carcinomata. Hyaline changes also may be present to a greater or lesser extent, and fatty degeneration and necrosis are not infrequent, while if extensive necrosis occur the connective tissue so affected may undergo calcification. Occasionally, in certain rare forms of carcinoma (osteoblastic carcinoma) the stroma regularly assumes the function of bone formation and nodules of more or less normal bony tissue are found scattered throughout the tumor (Plate XX, Fig. 4).

In addition to the purely degenerative conditions of the stroma there may be extensive inflammation, and this reaction may be of such an extent as to produce a true granulation tissue with numerous fibroblasts, so that the stroma resembles a sarcoma. Generally, however, such an appearance is produced by the spread of a carcinoma into the granulation tissue of an ulcer, the most frequent example occurring in the ulcerating carcinomata of the cervix uteri, where a large amount of soft spongy granulation tissue may be produced, through the spaces of which the cells of the neoplasm spread. While the stroma reaction is as a rule more extensive in rapidly developing tumors, even in slow-growing carcinomata, such as, for example, those of the skin, there is often a very extensive cellular reaction about the epithelium (Fig. 1203). These reaction cells, as a rule, are of the lymphocytic type, but occasionally large numbers of plasma cells (Fig. 1204) occur, spreading out along the tissue spaces. Rather frequent in some forms of carcinoma are numerous clasmatocytes, which are large, irregular, branching cells filled with granules

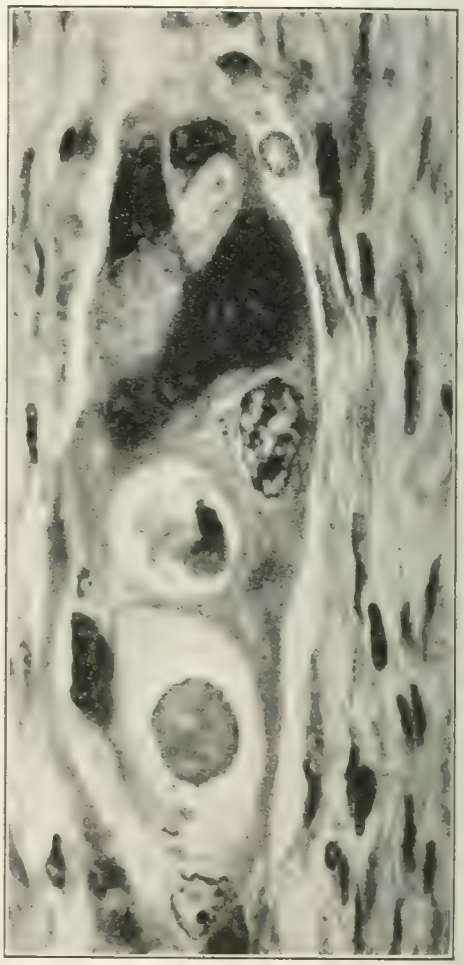


Fig. 1200.—Carcinoma of the Caput Coli. The section shows the spread of the tumor cells along the lymph spaces and the degeneration products inclosed in the epithelial cells. × 1000.

taking a basic stain. Phagocytic connective-tissue giant cells may also be found, especially about masses of necrotic material, calcified particles, or remnants of degenerating tumor cells, but this phenomenon is infrequent (Fig. 1205).

When a carcinoma invades muscle tissue there is usually some destruction of the fibers by pressure;

they become small and atrophic and undergo hyaline degeneration (Plate XXI., Fig. 3). There may be, however, some evidences of regeneration in the muscle fibers with the formation of large syncytial masses filled with nuclei, or the extremities of the fibers may become clubbed and the nuclei show mitotic figures.

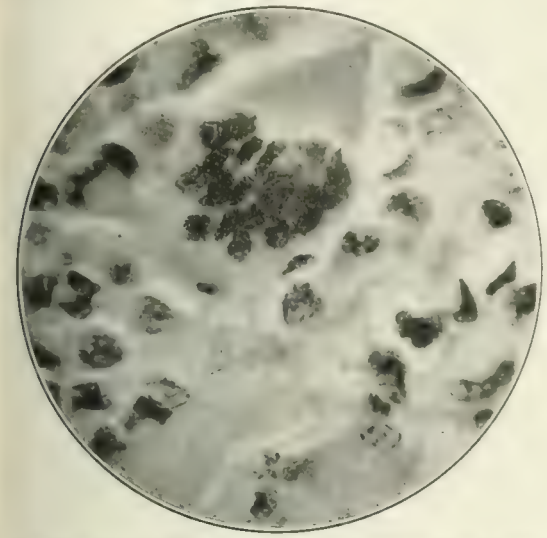


Fig. 1201.—Epithelial Tumor of Neck Showing Giant Cells. × 800.

The invasion of fat produces but little change (Fig. 1206); usually only a moderate lymphoid inflammatory reaction is found around the invading cells as a response to the irritation, though fibrosis and atrophy may occur.

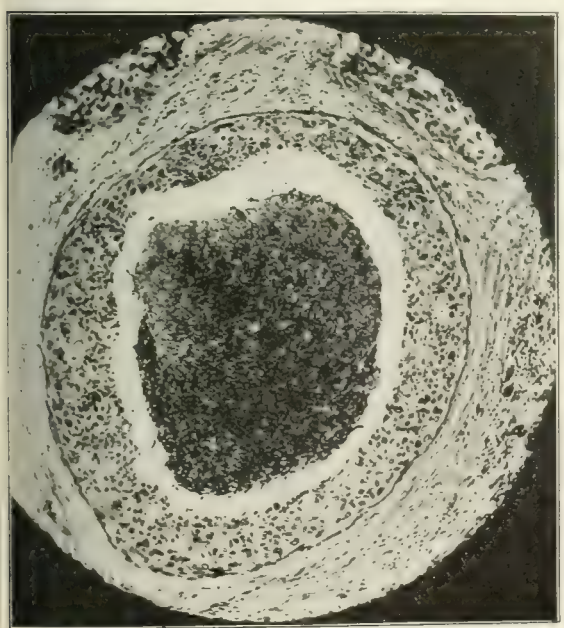


Fig. 1202.—Alveolus of Carcinoma with Central Necrosis.

The invasion of lymph nodes sets up a more or less vigorous reaction of the connective tissue, often with the formation of an abundant fibrous stroma. The blocking of the regional lymphatics with tumor masses may lead to dilatation of the peripheral node sinuses and the afferent lymph channels in the perinodular fat may be greatly distended with fluid, or both may contain embolic particles of carcinoma (Plate XXI., Fig. 4). Even the mere presence of a tumor usually incites an inflammatory reaction in the lymph nodes through

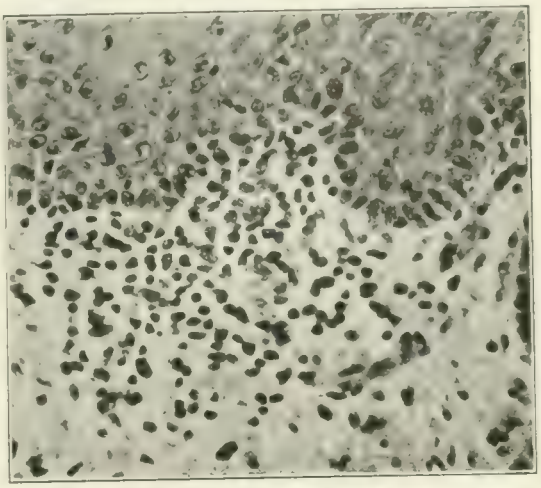


Fig. 1203.—Section from Early Epithelioma of the Lip to Show Subepithelial Infiltration in the Corium. × 400.

which drainage of the affected area occurs, though no carcinoma cells have entered the nodes themselves (Plate XXI. Fig. 5). This chronic inflammatory reaction is shown morphologically by hyperplasia of the endothelial cells in the central lymph cords and

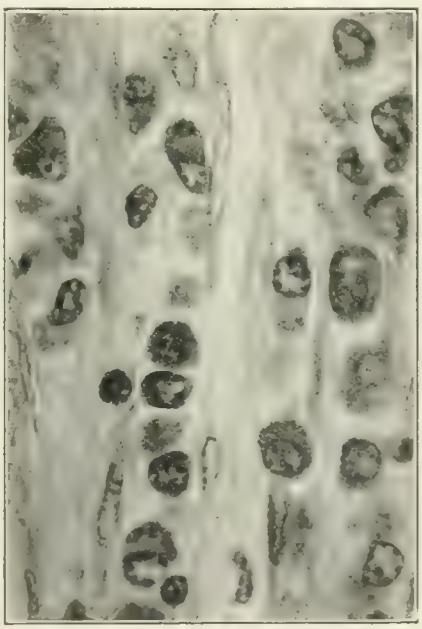


Fig. 1204.—Section of Connective Tissue near a Carcinoma of the Breast to Show the Infiltration with Plasma Cells in the Region of the Tumor. × 1000.

the peripheral lymph sinuses, and usually by a corresponding reduction in the normal quantity of purely lymphoid tissue. Occasionally the hyperplasia of the endothelial cells in the sinuses reaches such an extent that the cell masses somewhat re-

semble a carcinoma, a condition which may lead to the erroneous diagnosis of secondary metastatic deposits of carcinoma, when the condition is in fact purely one of response to irritation. Somewhat infrequently the stimulative action of the products

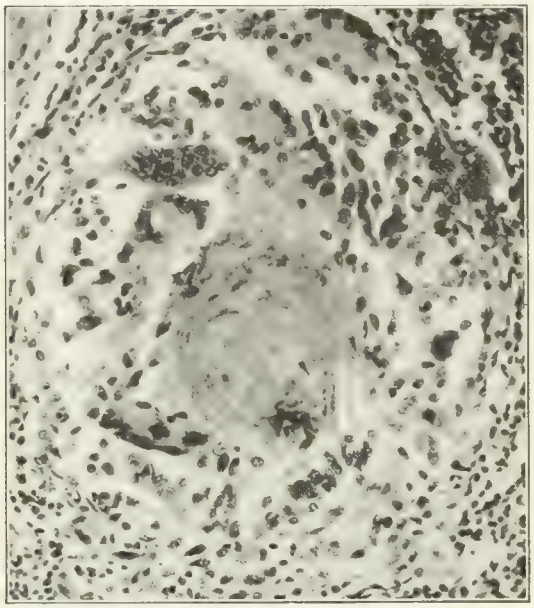


Fig. 1205.—Connective Tissue Giant Cells about Mass of Necrotic Epithelium near Secondary Epithelioma of the Submaxillary Lymph Nodes. × 375.

of metabolism or autolysis of the carcinoma cells induces the formation of small nodules of lymphoid tissue in areas in which no such tissue is normally present. Such lymph nodules have germinal centers and a peripheral meshwork filled with lymphocytes,

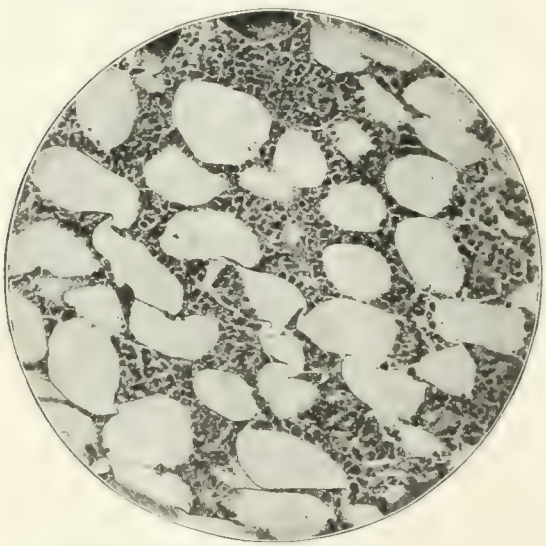


Fig. 1206.—Infiltration of Fat Tissue by Carcinoma Cells.

such as are characteristic of the normal lymphoid tissue elsewhere in the body. The formation of these nodules is observed most frequently in the tissue of the breast and axilla.

While as a rule the cells of a carcinoma invade the surrounding tissue through the lymph channels, an extensive involvement of the blood-vessel not infrequently occurs, with the result that embolic particles of the new growth are distributed throughout the body and may give rise under suitable conditions to the formation of secondary tumors. Such masses may undergo necrosis and disappear, but occasionally the tumor particle may become coated with fibrin from the blood stream and, thus protected from the destructive action of the blood, may develop a vascularized connective-tissue support from the vessel wall and extend as a cylindrical mass along the lumen.

When a carcinoma forms a metastasis in bone, or penetrates this tissue in the course of its growth, it

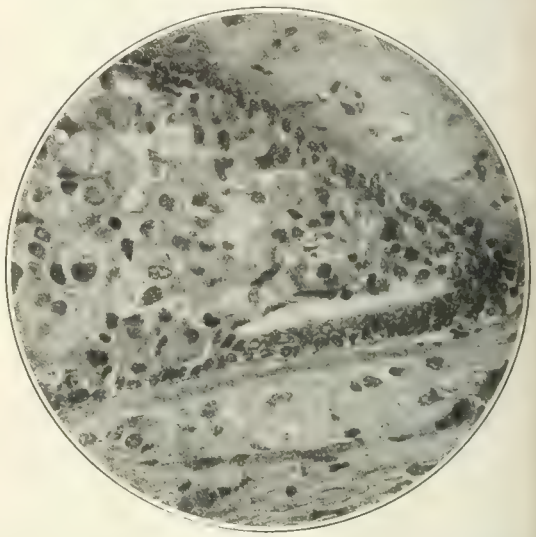


Fig. 1207.—Invasion of a Lacteal Duct by Carcinoma of the Breast. The epithelium of the duct is still present. × 400.

may produce no effect or it may cause either resorption of the bone, which is the usual phenomenon, or proliferation with very extensive production of osteoid tissue. Both processes may occur in various portions of the same tumor, the resorption of bone taking place in the usual fashion by osteoclasts or by simple decalcification without erosion, while in other portions new formation of bone may be observed. In the majority of instances, however, the process is in the direction of a diminution of the total amount of bony substance present, and clinical evidence of this is seen in the frequency with which fractures follow metastases of tumors in the shafts of the long bones.

Extension of carcinoma into the brain substance produces very little change. The tissue is simply pushed out of place by the new growth and undergoes circulatory alterations which result in the formation of a narrow necrotic area about the tumor, but no important lesions occur at a distance from the secondary deposit.

The invasion of nerve bundles is fortunately very rare, as this process is exquisitely painful; but occasionally, probably through the medium of the endoneural lymphatics, tumor cells penetrate a large nerve trunk and cause atrophy of its fibers with consequent sensory disturbances and paralysis.

The cells of tumors may invade normal skin or gland epithelium by contact, a phenomenon which has frequently given rise to the erroneous opinion that the normal epithelium has, under the influence of the contact, become carcinomatous (Fig. 1207). There is, however, no real evidence that such transformation can occur, and the general opinion is that the

EXPLANATION OF
PLATE XXI.

EXPLANATION OF PLATE XXI.

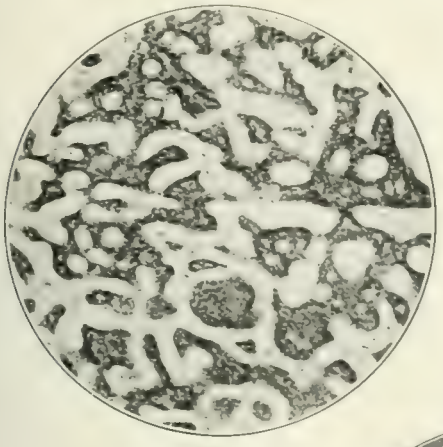
FIG. 1.—Cylindroma of the parotid. Low power to show the tubular arrangement. × 50.

FIG. 2.—Early carcinomatosis of axillary lymph node showing the invasion of the peripheral sinus. This was the only area in the node which showed any carcinoma. × 250.

FIG. 3.—Atrophy of muscle fibers due to the infiltration of carcinoma.

FIG. 4.—Embolus of carcinoma cells in a small lymph channel at the periphery of a lymph node.

FIG. 5.—Chronic hyperplasia of peripheral sinus of an axillary lymph node in carcinoma of the breast. × 375.



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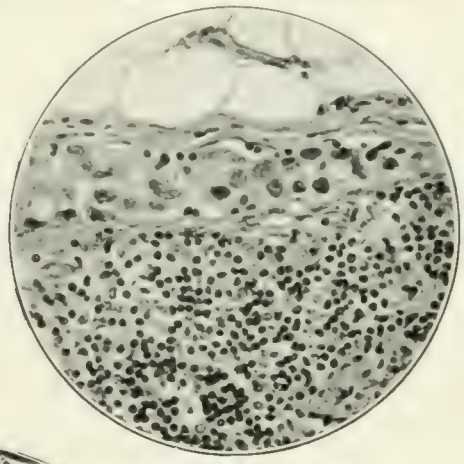

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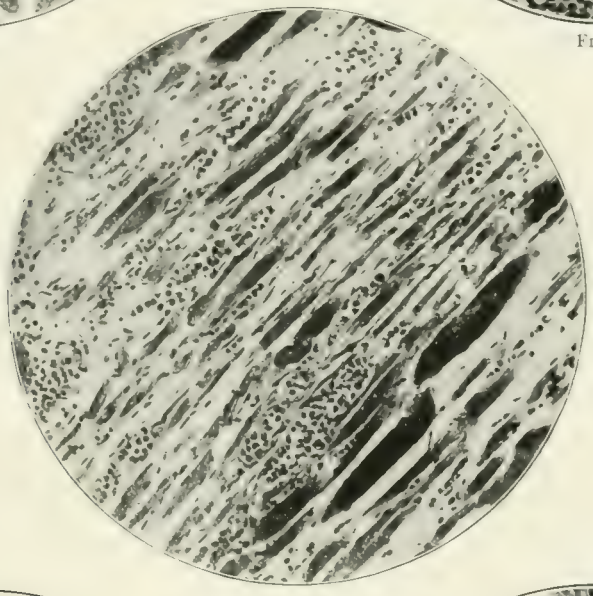

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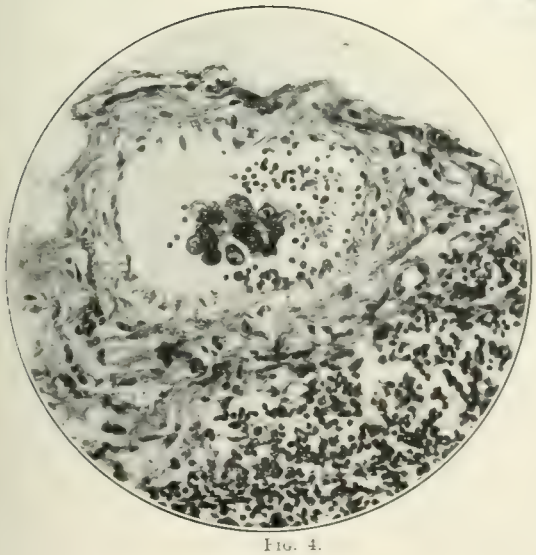

Fig. 4.

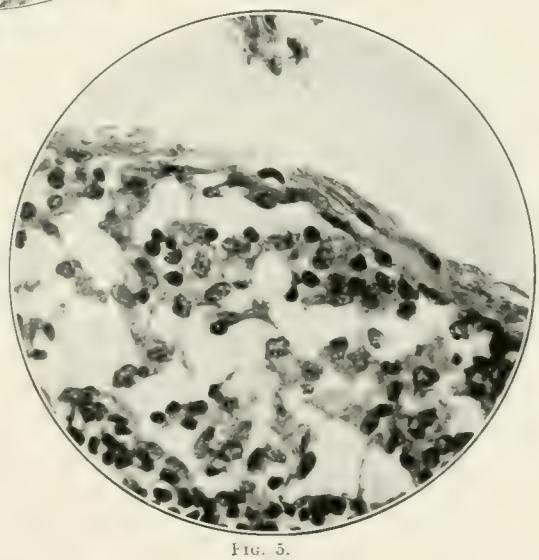

Fig. 5.

CARCINOMA.

carcinoma starts from a single center and grows peripherally. There is no reason to doubt, on the other hand, that in exceptional cases a carcinoma may begin in several centers, more or less distant from each other, and a study of certain multiple skin tumors (Janeway) has given considerable foundation for this belief. The simultaneous origin of tumors of different types in widely separated portions of the body also points to this possibility, as when, for example, carcinoma of the lip and carcinoma of the thyroid coexist in the same person, or a carcinoma arises in one part of the body and a sarcoma in another. But these cases are so extremely infrequent that they suggest the improbability of multiple origin as a general phenomenon, more than its frequency.

Invasion of the mucosa of the intestine by direct extension of a tumor of this viscus does not as a rule cause any very extensive changes (Plate XXI., Fig. 4). The structures of the intestinal mucosa are pressed aside by the growth, and the mouths of some of the glands may be closed, with consequent dilatation from retention of secretion; but no other changes may be noted. There may be edema of the interglandular connective tissue, however, sometimes with fairly extensive mucoid changes, and a considerable inflammatory infiltration of the submucosa and muscularis in the immediate region of the new growth may be observed with some regularity. Metastases in glandular organs are common. Secondary nodules in the liver are frequent; in the kidney and spleen they are much less often seen. The changes produced by the growth of metastatic nodules in such organs are relatively slight, and apparently are due largely to mechanical interference with the nutrition of the surrounding tissue. Metastatic nodules of carcinoma in the liver frequently show necrosis in their centers, and when protruding from the surface are often umbilicated. At the periphery of the nodule the liver cells are compressed, and necrosis may occur through the collapse of the smaller capillaries or their involvement by tumor cells, while there is often a moderate small cell infiltration of the neighboring tissues. If a very large number of metastatic particles have been carried to the liver through the circulation there may be numerous small areas of necrosis induced by the blocking of the terminal vessels with emboli of tumor cells. The growth of a connective-tissue stroma in metastatic tumors of the liver is an insignificant process only, and this is one reason for the early necrosis of these nodules. Occasionally, however, the secondary formation of a considerable amount of new fibrous tissue about the tumor particles may be seen. Changes in the kidney and spleen are in general similar to those described in the liver, and need not be detailed here.

The lungs frequently show secondary deposits derived from emboli of tumor cells which have lodged in these organs. Probably a large number of these disappear as a result of unsatisfactory nutritional conditions, but occasionally multiple tumors are produced throughout the lung, which, however, may cause relatively little disturbance. The cells either group themselves along the walls of the alveoli or form small, dense, miliary nodules which may perforate and grow freely on the pleural surface of the lung, or, finally, the emboli may cause infarcts or may interfere in other ways with the circulation. Metastases in the ovary are, curiously enough, fairly frequent even when the primary carcinoma is in the breast. Secondary invasion of the ovary may not cause any increase in size or alteration in form, or it may produce so large a tumor that the ovary is removed surgically because of the impression that it is the seat of the primary growth. Metastases take place in two ways: 1. Directly through the peritoneal cavity, which, of course, means either that the primary tumor involves one of the abdominal organs or that metastases are present in these organs and implicate the peritoneum. In such a case free tumor cells are, in all probability, carried by gravity to the ovary and other pelvic organs. 2. In another class of cases transportation of the emboli undoubtedly occurs by way of the blood-vessels.

Metastases in parts of the body other than those mentioned are infrequent. The skin (Fig. 1208) may show metastatic nodules, especially in hypernephroma of the kidney, and metastases have been described in the tonsils, the teeth, the heart muscle, the eye, the mamma, the uterus, and the suprarenals; although secondary deposits in these locations are rare. Metastatic growths have been found developing even in other tumors, for example, a metastatic nodule from a carcinoma of the prostate was found growing in a hypernephroma.

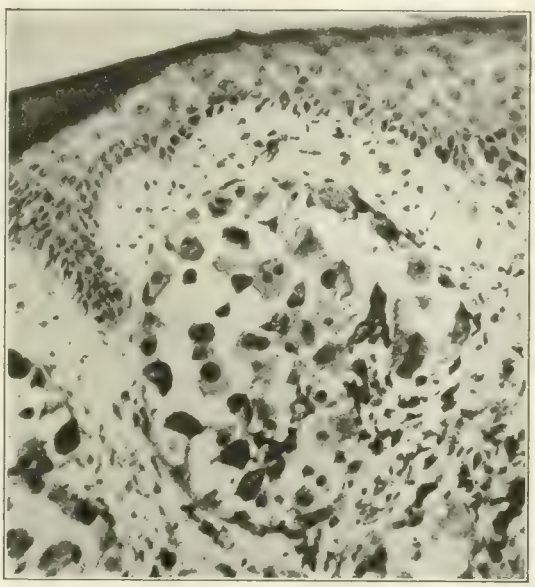

Fig. 1208.—Secondary Invasion of Skin by Carcinoma of Breast.

Mechanism of Metastasis in Carcinoma.—One of the biological qualities peculiar to malignant tumors is the power of producing metastases at a distance. Originally this appearance of secondary tumors was considered to be due to irritation by chemical products from the primary growth, or to the deposition of infectious particles, but careful microscopic studies of tissues showed long ago that neither of these views could be accepted, and the general opinion now is that the metastases are due to the transfer of individual cells or masses of cells by various means.

Lymphatic Vessels.—The most frequent route for the distribution of a carcinoma is through the lymphatic vessels, and upon this process there follows a secondary involvement of the lymph nodes of the region drained by these lymphatics. The factors which cause the cells to move along the lymphatics are as yet somewhat in debate, although in all probability the chief means is the transportation of the individual cells in the current of the lymph stream. Serial sections have shown that a single lymphatic trunk may show a series of deposits throughout its entire course with a final invasion of the peripheral sinuses of a neighboring lymph node (Plate XXI., Fig. 2.) Unquestionably the flow of the lymph, and, hence, the transfer of the cells, are hastened by muscular activity as well as by the intermittent pumping action of the respiratory movements in those situations where such

an influence can play a part. It has long been known that epithelial cells from a carcinoma have the power of ameboid movement (Carmalt), and this factor has been repeatedly insisted upon as important in metastasis; but whether the power of independent motion on the part of the cells is capable of transporting them over long distances is still in question. No doubt, the individual cells wander short distances through lymph spaces and form the so-called regional metastases which occur in proximity to the tumor, but distant lymphatic extensions are probably due chiefly to transportation by the lymph current. The fact that large cell carcinomata of the breast very rarely invade the axillary nodes, while a small cell scirrhus almost invariably does, is generally acknowledged, and points to direct stream transference, as the cells may be assumed to have equal ameboid capacities. When the regional lymph nodes are extensively invaded the cells of the carcinoma may pass out through the efferent lymphatics and enter and involve the thoracic duct, or be distributed immediately through this channel into the general circulation. General distribution throughout the body, however, usually occurs by direct invasion of the capillaries by the tumor cells and deposition of particles in the organs of the body. Such generalization of a carcinoma occurs much more frequently than is usually supposed, and may take place at a very early period in certain types of tumors, for example, eighty per cent. of carcinomata of the prostate, fifty per cent. of mammary carcinomata, and thirty-five per cent. of thyroid carcinomata (Kaufmann), are apt to form bone metastases at some stage of their growth; while vascular involvement by the so-called hypernephromata is more frequent than lymphatic transfer.

Blood-vessels.—If the cells of the tumor are small they may pass through the capillaries of the lungs and enter the general circulation; if the cells or particles of the tumor are large they are usually caught in the capillaries of the lungs and either form secondary nodules there or, as undoubtedly happens in many cases, undergo degeneration and absorption because the conditions are ill-fitted for continuous proliferation. While the blood of patients suffering from carcinoma is, as a rule, not so strongly cytolytic for the cells of their own tumors as is the blood of a healthy person for the cells of another person's tumor, yet some destructive action probably occurs when isolated particles are exposed to the blood stream. The organ in which the carcinomatous emboli are deposited is also a factor in their future development. The rarity of secondary nodules in the spleen as contrasted with the liver and lung points strongly to a relative tissue immunity in this organ.

Implantation.—A third method of transport is by direct extension or implantation. This is seen where tumors originate in or involve secondarily the large cavities of the body. The cells of the tumor under such circumstances grow continuously over the serous surfaces and form large plaques of new growth, often not extensively invading the underlying organs. A very frequent example of such implantation is seen in tumors of the ovary, and may occur even in some of the relatively benign cystadenomata. Sometimes this implantation is not in continuity but occurs only at a distance; thus, a small carcinoma of the stomach or gall-bladder not infrequently gives rise to such an extensive metastatic involvement of the ovaries that the primary tumor is overlooked. This condition has been recognized only recently as explaining the morphology of the so-called Krukenberg's tumor of the ovary, a growth in which the cells have the usual capacity of those from the gastrointestinal mucous membrane, for forming mucus-filled bodies which Krukenberg believed were characteristic of one type of primary ovarian tumor. Other types of contact implantation are noticed occasionally in transfers from one mucous surface to another, as when, for example, carcinoma of the upper lip gives rise to a similar tumor on the lower lip, or when uterine carcinoma forms metastases in the vagina, as happens not infrequently. Metastatic involvement of the bladder may occur by the transfer of particles from the kidney through the ureter.

Another form of implantation metastasis occasionally takes place after the puncture of carcinomata involving the internal organs, for example, the liver, ovary, peritoneum, and pleura, and following such a puncture a tumor may develop along the track by which the cannula was withdrawn. Metastatic growths of similar origin have been noted after incomplete operations on carcinomata involving organs in the abdominal cavity, and are especially frequent after the removal of ovarian carcinomata, when sufficient care has not been taken to avoid dislodgment of tumor cells and their escape into the field of operation. Experiments have shown that an animal which is the subject of a spontaneous carcinoma offers a much more favorable soil for the cells of its own tumor than for those of a growth derived from another animal. This explains the very frequent and diffuse local recurrences which often follow the imperfect removal of a carcinoma, and at the same time the infrequency with which convincing cases of the transfer of a malignant growth from one person to another have been reported.

While in general it may be assumed that metastatic nodules have the same capacity for progressive and diffuse growth as the original tumor, this is not always so, especially when, after the removal of the primary growth, the patient recovers somewhat from the malnutrition caused by the original tumor. Under these circumstances the carcinoma may entirely disappear from groups of affected lymph nodes or may remain quiescent for a long period; examples of inactivity extending over a period of fifteen years are not unknown.

Multiple Primary Carcinomata.—In the skin and the mucous membrane of the intestine, the development of multiple carcinomata is not infrequent. In the skin the condition is probably due to the action of similar irritative factors over large areas. It is probable, however, that multiple tumors of the intestine may often be explained in a different way, for they frequently arise from multiple congenital polypi.

Less frequent is the occurrence of tumors of two different types, as, for example, carcinoma of the lip and carcinoma of the thyroid, or carcinoma of one organ and sarcoma of another; though in the uterus carcinoma and sarcoma may occur together. A still more unusual occurrence is the combination of carcinoma and sarcoma in the same tumor, though a few neoplasms of this type have been observed in man. There is, however, always some risk in the interpretation of the nature of these so-called complex tumors, since the presence of carcinoma may give rise to a considerable proliferation of the surrounding connective-tissue stroma and the only certain criterion is that the mixed tumor produces metastases of two different types—sarcoma in one place and carcinoma in another. Observation of the mutation of animal tumors during transplantation, which has been seen in a number of cases where a carcinoma after repeated transfers has changed its type and becomes a sarcoma, has illuminated but not wholly explained the condition. It is possible that these neoplasms are mixed tumors from the start and that under different conditions of nutrition either the epithelial or the connective-tissue cells predominate in the growth. Some observers, however, consider that the change is the result of some unknown stimulus exerted by the epithelial portion of the tumor upon the connective tissue of the animal in which the transformation has occurred, with the ultimate production of a neoplasm of a sarcomatous nature.

Spontaneous Cure of Carcinoma.—While it is now generally acknowledged that carcinoma, both in man and in animals, can be permanently cured only by early and complete excision, it is not so generally appreciated that occasionally the spontaneous disappearance of a tumor may occur. This is not a frequent phenomenon, however, and Bashford has estimated that it occurs in less than one per cent. of mice with spontaneous tumors. Propagable growths, on the other hand, very often regress, and it is to a lack of appreciation of this point that many of the erroneous statements concerning the cure of mouse tumors have been due. Possibly, too, a few of the cases of cure reported in man may have been instances of spontaneous healing. Cases are on record in which carcinoma of the lip disappeared spontaneously, while metastatic nodules were still present in a lymph node, and the spontaneous cure of carcinomata of the skin has also been noted. Very suggestive in this connection is the disappearance of metastatic nodules in the lymph nodes occasionally observed after the excision of a primary tumor, and the checking of growth in a mammary tumor after removal of the ovaries is also an example of the influence of diminished nutrition upon growth, while the occasionally favorable action of radium and *x*-rays upon superficial tumors in man and in animals shows that the cancer cell has less resistance to these agents at least than the normal cell.

The great difficulty in obtaining a large percentage of successful inoculations from a spontaneous tumor into animals not immune also suggests that the cancer cell has not the vitality of normal epithelial cells, since it is always possible to transplant normal epithelium from one animal to another of the same species. The successful immunization of mice against the transplantation of carcinoma by the inoculation of mouse fetus epithelium is also interesting in this connection, for, as it is not possible to inhibit absolutely the taking of epidermal grafts in an animal by the injection of such fetal material, the cancer cell must be either more susceptible than normal epithelium or less able than a normal cell to use the nutriment offered by the tissues. Possibly another factor may play a part in the regression of tumors after the action of radium and *x*-rays, and also following the injection of certain substances, such as selenium, colloidal metals, or serum from a cancer patient. Radium and *x*-rays have, as is well known, a powerful action on the blood-vessels in inducing hemorrhage, endarteritis, and thrombosis. After injections of the substances mentioned above a marked congestion of the tumor and the surrounding tissue is often noted, and if the reaction is severe there may be a good deal of hemorrhage into the neoplasm. As the capillaries in carcinomata are very thin-walled and have no vasomotor nerves, there is no regulation against possible overdistention such as exists normally in the body. It is possible, then, that the toxic action of the substances mentioned may so injure the delicate walls of the vessels that extravasation of blood may occur with ultimate necrosis of the tissue thus deprived of its nutriment. The softening which has been observed during spontaneous regression or after one of the forms of treatment mentioned, occurs in the central portion of the tumor where the blood supply is most meager, and not at the periphery where the vessels of the connective-tissue reaction zone are relatively large and thick-walled.

Action of Carcinomata on the Organism as a Whole.—The presence of a malignant epithelial tumor, if this be small in size and of slow growth, may not interfere in the least with the nutrition of the patient nor immediately endanger life. It is well known that some of the epitheliomata of the skin grow so slowly that they do not assume serious proportions for ten or even twenty years. There are on record also certain tumors of the breast with an extremely prolonged existence without the formation of metastases or extensive local involvement. In such cases the body nutrition is only very slowly altered, if it be affected at all. Tumors involving important organs of the digestive system, however, interfere rapidly with nutrition, and the condition of cachexia supervenes. This is characterized by a general diminution of the bodily powers, often with a severe secondary anemia and a negative nitrogen balance as evidenced by continuous loss of weight or more accurately by careful metabolic estimations and the appearance in the urine of large quantities of certain sulphur-bearing substances known as oxyproteic acids. Changes in the antitryptic power and variations in surface tension of the blood serum have been found in many cases but are not characteristic of the cachexia of carcinoma. The gastric juice loses its free acid and even its ferments in a considerable proportion of these cases; whether the pancreatic and intestinal secretions are also interfered with is not as yet definitely known. While it is probable that the chemical composition and the metabolic products of the carcinoma cell may differ slightly from those of normal cells, it has not been possible as yet to demonstrate any specific toxic agent derived from these elements. It has been repeatedly stated that the metabolic products of tumor cells are hemolytic, but the power to dissolve red blood-corpuscles is a property which is inherent in extracts of certain normal gland cells of the body and even the blood serum of normal people is frequently lytic to foreign red blood-corpuscles. In this connection, however, it should be remembered that very little or no anemia may occur with large and even ulcerating carcinomata provided the digestive functions are not interfered with. How much of a rôle is played by the psychic depression from knowledge of the serious nature of the disease it is difficult to determine. It has often been observed, however, that following a very simple surgical interference which does not in the least alter the rate of growth of the tumor there may be quite a marked improvement in the general condition of the patient. Such an occurrence has often been noted following gastroenterostomy to relieve pyloric stenosis, or colostomy done to remove obstruction due to new growth of the sigmoid flexure or rectum, despite the continued growth of the tumor. This change is largely due, no doubt, merely to improved digestion and absorption of food with consequent favorable influence of nutrition. It has not infrequently been observed that the gastric juice regains its free acid and its full ferment content after such a palliative operation. At the present time, therefore, the question whether the cachexia is due directly to the mere presence of a tumor must be regarded as undecided.

F. C. Wood.

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Carcinoma, Clinical.—See *Cancer*.

Carcinoma of the Skin.—In the present article carcinoma is employed as a comprehensive term embracing all the varieties which have their starting-point in the surface epidermis or its appendages.

The most satisfactory classification is based on histological types which correspond approximately with clinical pictures.

Cutaneous carcinomata in the great majority of cases take their point of origin from the epidermic covering or the sheath of the follicles, the glandular epithelium only exceptionally proliferating primarily. Although there are many classifications based on the microscopic or macroscopic appearances, relative malignancy or genesis, the histological division of cutaneous epitheliomata into two great groups, according to certain prominent characteristics is the most practical, namely, the prickle-cell group, and the basal-cell group of Krompecher. In the former, the tumors are composed of large cells which have retained their prickles; they are early destructive, metastasize, and have a general malignancy. In the basal-celled group the tumors are made up of small cells which possess no prickles and have relatively large nuclei; they do not as a rule metastasize and have usually only a local malignancy. While recognizing the validity of the criticism made by Adami that all cells originate from the basal layer, it is nevertheless a fact that in the one case only one type of cell continues to proliferate while in the other differentiation goes on. As a rule, too, these two types conform more or less with distinct clinical pictures, though occasionally cases are seen in which a positive diagnosis can be made only by the microscope. Patients with multiple epitheliomata sometimes present the two types with not sufficient clinical differences to tell them apart.

An important fact to be borne in mind is that carcinomata of the skin are not infrequently multiform in their manifestation and often have a relatively benign course.

Varieties.—*Superficial Epithelioma; Rodent Ulcer.*—One of the most frequent forms in which carcinoma of the skin begins is as a small, hard, pearly gray nodule generally found on the upper two-thirds of the face in individuals over forty years of age. These nodules are often multiple, may remain for years with little or no change, or even may disappear spontaneously. If they are removed during their primary stage before ulceration begins they show only a slight tendency to recur.

After a time one or more of these small growths may slowly increase in size, the center at the same time sinking in and eventually becoming fissured or excoriated as the result of scratching or other irritation. At this stage, the new growth consists of a superficial ulcer covered with crusts made up of blood and secretions from the affected surface, and surrounded by a hard, elevated, waxy looking margin (Fig. 1, plate XXI.). The central ulceration may heal but is sure to recur, each time becoming somewhat larger, but seldom involving the deeper tissues; it has a red, granular base, secretes but little pus, and rarely causes pain. The floor and edges of the ulcer, consisting of soft friable tissue extending beneath the overlying epidermis, are easily removed by the curette. Instead of extending in a regular and progressive manner the ulceration may heal in the center while continuing to spread at the margins, or one side may cicatrize, as a result of which gyrate and irregularly outlined ulcers with new foci may develop in the scar tissue. Such a carcinomatous ulcer may generally be differentiated from syphilitic or lupous ulceration by the presence of the elevated, waxy, or pearly gray margin.

A frequent site of rodent ulcer is near the inner canthus or the side of the nose. The small pearly nodule, which marks the beginning of the affection breaks down in the center and slowly spreads, involving the upper and lower lids and at times destroying the eye. For many years the characteristic rolled pearly margin is preserved but eventually this characteristic feature of the growth disappears. Fig. 1 illustrates such a growth.

The progress of the affection is excessively slow, lasting ten, twenty, or even forty years before the patient dies from this or some other malady. It may eventually, however, invade the orbit, destroy the greater part of the skin of the face, the malar bones, the upper jaw, and penetrate the skull, causing the death of the patient from hemorrhage, exhaustion, or the involvement of vital organs. Fungating tumors reaching a considerable size may spring up from these ulcerating surfaces.

Fig. 1209.—Rodent Ulcer of the Inner Canthus Involving the Upper and Lower Lids, and Showing All of the Typical Clinical Features of the Affection.

In addition to the early lesion in the form described, epitheliomata about the face may begin as brownish-red tubercles, hemispherical in outline, quite smooth, and of medium consistence. If undisturbed these nodules grow slowly for a number of years, then, under the stimulus of some irritant, increase more rapidly in size, finally resulting in open ulcers.

Disseminated Epithelioma of the "Sebaceous Type."—Multiple epitheliomata which are met with especially about the face, sometimes on the hands and trunk, are usually preceded by certain definite changes in the skin to which the name "senile keratosis" has been applied (see *Keratosis Senilis*).

In Paget's disease of the nipple a superficial, moist, crusted, slightly scaling dermatitis may exist for a number of years as a precancerous condition. Healing cannot be brought about by the ordinary applications and eventually a superficial or deep-seated carcinoma appears in or beneath the chronic dermatitis (see *Paget's Disease*, under *Breast, Diseases of*). Superficial flat epitheliomata strongly resembling typical Paget's disease of the nipple occur on other portions of the body. They have an eroded granular center, a slightly rolled polycyclic margin, and in certain cases the same histological structure as in true Paget's disease.

Multiple epitheliomata at times develop on old patches of psoriasis. The prolonged use of arsenic in this and other chronic skin diseases may be followed by patches of keratosis and horn-like lesions especially on the palms of the hands and soles of the feet, beneath which cancerous ulceration begins. These malignant changes are usually multiple, and in fifty per cent. of the cases recorded they developed before the age of forty. Among arsenic miners

carcinoma, beginning as arsenic warts on the fingers, has not infrequently been observed.

Chimney-sweeps' Cancer of the Scrotum.—This variety of cancer, which at one time was often met with in England, has become less frequent since the enforcement of laws forbidding sweeps to ascend flues (see *Scrotum*).

Tar and Paraffin Cancer.—Volkmann first called attention to the occurrence of cancer of the scrotum and forearms in workers in coal tar and paraffin. The antecedent changes in the skin are similar to those met with in chimney-sweeps' cancer. The follicular openings are occluded, the skin becomes dry, thickened, and the seat of warty growths which subsequently become malignant.

Chronic affections of the derma, as lupus, syphilis, etc., seem to favor the development of carcinoma by lessening or removing the normal barrier which separates the epithelium from the connective tissue. At the same time a constant irritation is exerted on the epithelial layer which causes it to undergo hypertrophy and ultimately may lead to its becoming the seat of a malignant growth. Carcinomata develop from active lupus or from its scar tissue so frequently as to indicate more than an accidental relationship. Some authors speak of lupus-carcinoma as a clinical and pathological entity.

Syphilis of the tongue is one of the most frequent precancerous affections of this organ. Late syphilitic neoplasms, interstitial glossitis, and leucokeratosis may be followed by rapidly growing carcinomata. Indifferent scar tissue of the skin, when exposed to long-continued irritations, forms a favorable soil for the development of a malignant tumor. The course of such growths is less rapid than when they start from the scar tissue of lupus. In the latter case there is nearly always more or less active tuberculous disease and thus less resistance is offered to the epithelial ingrowths.

Papillary Carcinoma.—In various localities cancerous ulcers, like ulcers of any sort, may show a marked hypertrophic tendency, which results in the formation of cauliflower-like excrescences. These arise from a joint proliferation of the rete Malpighii and papillary layer of the corium. Such growths are commonly encountered on the lips, penis, scrotum, scalp, ears, cheeks, etc. In some instances this papillomatous proliferation occurs in advance of ulceration, so that the epithelioma begins with a wart-like outgrowth, as mentioned elsewhere. These cauliflower-like growths are not essentially more malignant than other forms, although they may bleed readily and discharge freely; but in certain cases they may attack the deep structure in a manner seen in non-papillomatous forms. The tendency to proliferate eventually disappears and a complete destruction of all the involved tissues results.

Nevus-carcinoma.—These growths are so closely identified with sarcoma, especially the melanotic form, that they are best considered under the head *Sarcomatosis cutis*.

Deep-seated or Nodular Carcinoma.—The great majority of cutaneous cancers conform to one or more of the types which have been described and are in their early stages more or less superficial. Many preserve such a location during their entire evolution, the new growth ulcerating as soon as it develops. Others may early tend to involve the deeper tissues, giving rise to distinct indurations or veritable tumors which invade the muscles or bones. The deep-seated or nodular carcinoma is, therefore, usually secondary to a surface ulceration, but it may occur near the cicatrices of former operations for malignant disease, a group of cells in the subcutaneous tissue acting as a focus for the relapsing growth.

Metastatic cancers of the skin from visceral or breast carcinoma are usually first detected as small subcutaneous nodules which, in exceptional cases, may enlarge, assume an irregularly rounded shape, and become firmly attached to the underlying tissues.

Carcinomatous Lymphatic Infarction.—This is the name given by Unna to a sub-form of cancer of the skin. It is generally described as lenticular carcinoma. It is met with, in the great majority of cases, in the skin covering the female breast as a development secondary to mammary carcinoma; it may also develop in the cicatrix following operation for cancer of the gland. Epithelial cells from the primary growth are conveyed by the lymph vessels and give rise to the formation of small white or pinkish papules from the size of a small shot to that of a pea. Infiltrated patches at times result from the confluence of numerous primary nodules which may or may not undergo ulceration.

When the lymphatic infection is active and extensive the entire cutaneous surface over the front and back of the chest may be involved, the process even extending to the skin of the abdomen and arms. In the later stages the skin becomes hard and leathery in consistence from the growth and contraction of the connective tissue, producing the condition known as *cancer en cuirasse*.

The constriction produced by the new growth may be sufficient to interfere with respiration or may give rise to edema of the arm from interference with the lymph circulation. A fatal result may follow within a few months after such a development occurs, but in certain cases general infection is delayed for a number of years.

Carcinoma of the Sweat Glands.—The most divergent opinions exist as to the rôle played by the sweat glands in tumor production. Certain pathologists at various times have attempted to show that many small-celled epitheliomata, in which the cells grow in tubular processes, have such an origin. It has, however, been clearly demonstrated that neither the shape, size, nor arrangement of the cells furnishes sufficient criteria on which to base the diagnosis of sweat-gland cancer.

The author of the present article some years ago examined a tumor which had been removed by Dr. Bronson from the anterior surface of the leg of a man thirty-five years old, and which proved microscopically to be a carcinoma originating in the coil gland. The growth in question was composed of distinct lobules, separated by the ingrowth of connective tissue; it was soft to the feel, about half the size of a small egg, and defined from the surrounding tissue without being distinctly encapsulated. It extended about one inch below the skin, and measured an inch and a half in its long diameter. An open ulcer, somewhat larger than a dime, was present over the tumor. The cancerous nature of the new growth was not suspected prior to the microscopic examination.

Neither the duration of the tumor nor its onset as a surface or deep affection was noted.

Carcinoma of the Lip.—Cancer of the lip, by reason of its frequency, malignant course, and the importance of an early diagnosis, demands a separate consideration. Its seat of predilection is the lower lip, at the junction of the skin and mucous membrane near the median line. It may occur near the angle of the mouth. The development of a tumor on the upper lip has been noted in one or two instances. In these cases contact with the primary growth on the lower lip may have served as a cause. Cancers of the upper lip, as a rule, occur at some distance from the vermilion border and are usually of the rodent ulcer or superficial type of growth. When the mucous membrane is involved by the extension of such a tumor of the upper lip its clinical course differs from that of the typical cancer of the lower lip. It does not penetrate deeply nor infect the lymph nodes as in the latter case.

A number of primary changes in the surface epithelium may precede ulceration or tumor formation.

Hyperkeratosis over a limited area, followed by a fissure and later by ulceration, is often observed. The ulcer is irregular in outline and surrounded by thickened and elevated margins. The base of the ulcer becomes indurated and the infiltration gradually extends to the deeper tissues.

In another case the epithelium may become eroded instead of thickened and covered by closely approximated granulations which enlarge until they assume a warty character. This papillomatous growth may

Fig. 1210.—Epithelioma of the Lip. The new growth is in striking contrast to the conditions met with in rodent ulcer.

spread laterally until almost the entire lip is covered with granulations before deep extension takes place. Instead of the ragged ulcer, a shallow, oval and regularly outlined loss of tissue may constitute an early form of lip cancer.

Changes in the epidermis may be overlooked and the patient's attention may be first directed to a hard growth below the surface. This soon ulcerates, leaving a cavity surrounded by hard walls and base from which the degenerated epithelial cells forming the center of the epithelial "pearls" may be squeezed out as comedo-like bodies. In certain cases of epithelioma of the lip a projecting tumor is formed which may last a variable time before it breaks down by ulceration. Fig. 1211 illustrates this condition.

In neglected cases the infiltration and ulceration involve the entire lower lip and the floor of the mouth; the teeth become loosened and all the adjacent tissues are destroyed. The submaxillary and submental lymph nodes are involved, as a rule, before such extensive tissue destruction occurs. The average duration of life in untreated cases is from three to five years, death taking place from sepsis or metastasis.

Cancer of the lower lip occurs in about fifty per cent. of surface epitheliomata. The male sex furnishes an overwhelming percentage of all cases, variously estimated at from eight to one to twenty to one. Statistics show that the large majority of those so afflicted are addicted to the use of tobacco, and of the few cases met with in women three-quarters were smokers.

Diagnosis.—The initial lesion of syphilis is often mistaken for cancer of the lip. Chancres of the lip are usually protuberant with an eroded or encrusted surface; they develop rapidly and very early involve the lymph nodes. The initial sore of syphilis is more likely to be met with in young adults, while epithelioma is a disease of later life. Numerous exceptions to these rules, however, are found.

Late ulcerating syphilides of the lip have also been mistaken for cancer, but these neoplasms of syphilis are usually multiple, rapidly break down, or undergo absorption with atrophy, and lack the hard base which is always present in cancer.

In a doubtful case appeal should be made to the microscope.

Prognosis.—The course of carcinoma of the lip is much more rapidly fatal than is that of the flat variety of epithelioma of the skin. An early and radical excision by the knife is the only method of treatment which promises subsequent immunity to the patient. If the operation is performed while the affection is superficial the outlook is not unfavorable. Even in such cases early operations sometimes fail to prevent general infection.

Pathology and Morbid Anatomy.—In respect to classification histologically, the typical feature of squamous-celled growths is the solid prolongations or downgrowths from the epidermis, which spread out in different directions or on section give rise to masses of alveoli of various shapes and sizes lying in a connective-tissue stroma. In the characteristic members of this group the epidermal characters are preserved and result in epithelial pearls.

Fig. 1211.—Squamous-celled Epithelioma (Zeiss 8 mm., Comp. Oc. 4). Showing downgrowth from the surface epithelium and alevoli with pearl formation.

In tissue undergoing malignancy certain changes take place which indicate the vegetative activity of the cells. These are a smaller cell with oval or rounded cell body, clear cytoplasm and a relatively large, deeply staining nucleus; the relations of the cells to one another become changed, they become crowded and occupy a much smaller space than under normal conditions. This is especially true of the basal-celled tumor and it is not so difficult to make a diagnosis in these cases of early epithelioma. In the squamous-celled type, however, particularly those which develop on ulcerated surfaces, it is not so simple to say whether one is dealing with tumor formation or only atypical proliferation. In chronic ulcerations there is a marked tendency for the epithelium at the edges of the ulcer to grow irregularly downward and infiltrate the tissue beneath. These processes may become snared off and sometimes develop pearls, when it is practically impossible to

EXPLANATION OF
PLATE XXII.

EXPLANATION OF PLATE XXII.

The colored pictures have been made from photographs of the author's cases.

FIG. 1.—Early stage of superficial epithelioma of the face, the so-called rodent-ulcer type of the affection.

In this variety of epithelioma the new growth is made up of small epithelial cells which correspond to those in the basal layer of the epidermis or in the outer root-sheath of the hairs.

The growth began in this case as a small pearly gray nodule which slowly ulcerated in the center while spreading with an elevated margin. The progress of this type of epithelioma is exceedingly slow.

FIG. 2.—A more advanced stage of epithelioma of the skin. The growth here portrayed is of eight years' duration. It began as a wart which rapidly spread after the application of some caustic. The postcervical lymph nodes were enlarged. The microscope showed the tumor to be a squamous-celled epithelioma, the prognosis of which is more grave than that of the rodent-ulcer type.

FIG. 3.—The tumor here shown was seen when fully developed on the scalp of an old woman. It was attached by a broad peduncle, its margin resting on the healthy skin. The body of the growth was made up of moist, warty vegetations which readily bled on slight irritation. Under the microscope the tumor was found to resemble an alveolar carcinoma, the connective-tissue framework being rich in newly developed blood-vessels.

FIG. 1. EARLY STAGE OF RODENT ULCER OF THE FACE.

FIG. 2. SQUAMOUS-CELLED EPITHELIOMA OF THE SKIN.

FIG. 3. PAPILLARY OUTGROWTH WHICH DEVELOPED ON EPITHELIOMA OF THE SCALP.

CARCINOMA OF THE SKIN.

determine from the histology the exact pathological condition.

Of the basal-celled epitheliomas the rodent ulcer may be taken as the type, as it is the form most frequently met with. These tumors are made up of an undifferentiated type of cell, yet, contrary to the rule, are the least malignant of epithelial tumors. Various degrees of anaplasia are met with and a more or less spherical, polygonal, or even spindle-shaped cell may be encountered. Not only the cellular morphology but the general structure of these basal-celled tumors varies and has led to the recognition of certain well-defined types. It has been suggested by Darier that this varied architecture might be explained as the attempt on the part of the basal layer to functionate, as during embryonic life, in the production of the appendages of the skin.

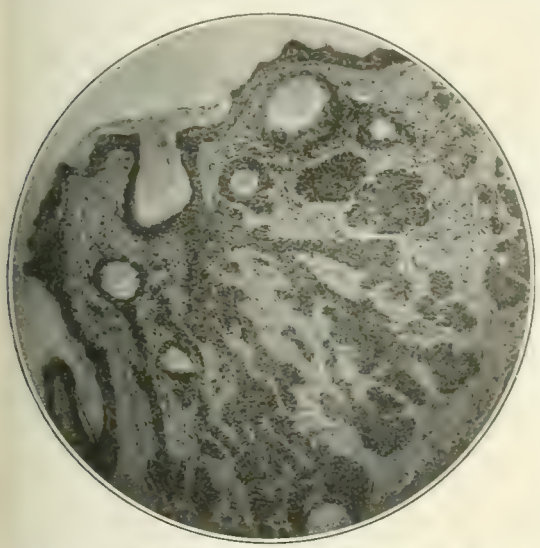


FIG. 1212.—Rodent Ulcer (Zeiss 8 mm., Comp. Oc. 4). An early rodent ulcer near ala of nose, taking its origin from the lanugo hair follicles.

The picture of the ordinary rodent ulcer differs a great deal in appearance and may, in one instance, appear as a solid downgrowth from the surface epithelium, with little tendency to branch; in another the larger masses may show central cystic degeneration and peripheral budding, or fine or coarser processes of cells bifurcate throughout the cutis. Trichoepithelioma, which develops from lanugo hair follicles, has a somewhat different structure, which may be due to an attempt on the part of the cells to differentiate. These growths clinically may appear as morphea-like lesions, as already described.

A frequent concomitant of the basal-celled tumor is the hyaline or mucinous degeneration, which affects either the cells or the connective tissue, or both. Degeneration is considered by some authorities, as Adami, to indicate malignancy, but in the skin we find the tumors most prone to degenerate are of a benign type. In mucinous or pseudomucinous degeneration the cells appear indistinct and poorly differentiated, in areas breaking down and forming cystic cavities which contain the products of degeneration. Aside from these changes there may occur a central autolysis of cells (Adami) which may be due to lack of nutrition or to metabolic products of the tumor cells themselves. Extractives or diffusible products *in vivo* may have the same effect in producing this autolysis as the introduction of a vaccine from a tumor.

Sweat-gland Cancer.—The case of sweat-gland cancer which came under the observation of the writer and to which reference has been made, had the following histological structure: Under a low power the derma was found to be the seat of numerous bands, masses, and gland-like arrangements of small epithelial cells which extended from beneath the epidermis to the subcutaneous connective tissue. They differed in their arrangement from that met with in other varieties of skin cancer, and suggested to the observer an attempted reproduction of glandular tissue. Under a higher amplification a complicated network was seen; it was formed by the interlacement of bands of epithelial tissue enclosing cavities which were partially or completely filled with degenerated cells or with a homogeneous substance allied to colloid matter. Cyst-like cavities were found in other parts of the microscopic field. They were lined by a single layer of columnar epithelial cells, and presented a striking resemblance to overgrown sweat ducts.

ETIOLOGY.—The epidermis is susceptible to stimulation by a variety of influences. This is seen in the large number of dermatological affections which are accompanied by abnormal proliferation of the epithelium. In the majority of these the proliferation remains within the bounds of an inflammatory process, but not at all infrequently malignancy intervenes. What is the factor that gives rise to the initial impulse? By the investigators interested in this subject it is believed that this impulse is stored up in the nucleus. So long as a cell is engaged in the performance of its function it uses up its energy and cannot at the same time conserve energy for proliferation (Adami), but with a disturbance of function conditions are changed and the vegetative powers of the cell gain the ascendant.

Recapitulating briefly some of the factors which stimulate epidermic cells, microorganisms like the staphylococcus, or its toxins, may produce such an overgrowth that large areas of skin, as of an entire extremity, are converted into a fungating mass. This is sometimes met with in dermatitis vegetans. In tuberculosis verrucosa, in which the tubercle bacillus gains entrance through the skin, the tissue is excited to warty hyperplasia, whereas in the other forms of cutaneous tuberculosis the epidermis is but little altered. In yaws the *Spirochæta pertenuis*, which is constantly found between the epithelial cells, produces a lesion consisting of marked epithelial hyperplasia, which gives the disease its peculiar characteristics. In syphilis, leucoplakia and condylomata are striking examples of epidermic proliferation. The enormous fungations accompanying blastomycosis are probably the result of the reaction of the epidermis to the blastomycetes, that being their portal of entry. Molluscum contagiosum, common warts, and Darier's disease are further illustrations of acanthosis; although the nature of the respective stimuli is not determined.

Chemical substances like tar and paraffin, arsenic, tobacco, scarlet red, etc., likewise possess the power to excite epithelial growth. From tar and its derivatives we may have all grades from a mild stimulation leading only to overgrowth of the horny tissue, as in the acne lesions, to multiple malignant tumors. Between these stages may be seen the development on telangiectatic patches of flat warts in which malignant transformation takes place.

As a result of the prolonged administration of arsenic, certain changes are brought about in the skin which result in pigmentation, scaly patches and warts or keratoses, with epithelioma as a sequel. The injection of various substances in the skin of animals has been followed by epitheliomatous development, as shown by the experiments of Fischer and Stober with scarlet red. Indol, skatol, and other products of intestinal fermentation injected into the ear of a rabbit

by Stoker and Wacker also brought about a reaction indistinguishable from carcinoma.

Of the physical agents, light is one of the most important factors in its power to induce certain changes in the skin which lead to epithelial proliferation. We are largely indebted to biological research for our knowledge of the potency of this energy and its good and evil effects. From investigation on the elementary forms of life it has been ascertained that the properties of the protoplasm of these organisms may be completely modified by the action of light energy, causing them to assume new forms and even so change the conditions of existence that an aerobic organism may become anaerobic under its influence. From his observations on the heliotropism of plants, Sachs formulated the law that light of constant intensity acts continuously as a source of stimulation. A heliotropic action on the part of animals in accordance with that observed by Sachs was also demonstrated by Jaques Loeb. The effect of light on the normal skin is an erythema, acanthosis. and thickening of the corneous layer. Its relation in the production of pigment is too well-known to claim more than passing mention. It has, further, been demonstrated that it is the short waves—the blue and ultra-violet rays—which constitute the pernicious element in the production of pathological conditions. These actinic rays acting on a senile skin, or that of persons exposed to the weather, as sailors, are capable of producing such changes as telangiectases, pigmentations, atrophic lesions, and warts, one or more of which may become malignant. The telangiectatic and pigmented lesions are the processes of defense on the part of the organism to protect itself against their injurious effect. Difference in susceptibility is a matter of every day observation. This is seen in the freckling of a supersensitive skin and in the way different people react to sunburn, it being mild in one case and intense in another. In xeroderma pigmentosum changes are found identical with those met with in the senile skin, light exciting the same syndrome of symptoms as in the aged. The primary condition is a congenital defect of the skin either local or due to some internal cause (Loeb) which renders the integument vulnerable to the action of light and brings about in it a precocious senescence. The *x*-ray in its effects is similar to solar light. On the normal skin its action is to interfere with secretion and the function of the cells, and if prolonged it results in degeneration and destruction, finally leading to new growth.

Observation of facts like these favor the view that the essential stimulation to epithelial growth may be multiple, in one degree leading to a limited increase of cells and in another to lawless growth, the amount of stimulation or the susceptibility of the individual determining the result. The study of the sections of pre-epitheliomatous changes in the cell would favor the view that it is in the cell nucleus that the first effects are produced, probably in the chromatin loops, which possess vegetative and specific function, as suggested by Oertel. With the loss of the essential secreting function there is an exaggeration of the vegetative power. In the breast, for example, when the capacity to secrete milk is suppressed the cells may become vegetative and proliferate, although this may happen in the active stage of the gland. Similarly in the liver and stomach when functional activity is interfered with the vegetative properties of the cells preponderate.

Skin cancers afford much evidence that they start from degenerated cells, as in leucoplakias, keratoses, degenerations brought about by light, solar ray, and *x*-rays, chronic inflammatory processes, etc. Many of our dermatological observations, therefore, fit in with Oertel's theory as we may see cells proliferate in close proximity to degenerated ones.

Diagnosis.—Superficial cancer of the skin is frequently mistaken for late syphilitic infiltration and ulceration or for lupus. These late nodular and ulcerative syphilitic lesions are usually more rapid in their evolution and involution, are frequently multiple, and lack the characteristic elevated and waxy border which distinguishes malignant ulceration. When syphilitic ulcers or those of lupus are complicated with epithelioma the diagnosis is more difficult. Lupus generally develops early in life, pursues a chronic course, and spreads on the margins of the patch by brownish-red nodules deeply embedded in the skin. These nodules or tubercles are as characteristic of lupus as the waxy margin is of superficial epithelioma.

Tuberculosis verrucosa cutis might be mistaken for papillary cancer of the fingers or hands. Induration about the base of a wart or cutaneous horn should excite suspicion of a malignant change.

In case of doubtful diagnosis resort should always be made to the microscope.

Prognosis.—In superficial cancer of the skin the prognosis is more favorable than in any other form of the disease, as the progress is slow and the lymphatic system seldom implicated. If the growth is radically removed in its early stages there is little tendency to recur.

Cancers from moles are decidedly malignant, as they early involve the lymphatics and may soon be followed by a general metastasis. Papillary cancers are usually rapidly growing, and when they infiltrate the deeper parts, if not removed, lead to a fatal issue within from one to three years.

Rodent ulcer in its later stages almost invariably returns after removal, though preserving its local seat.

It is well to bear in mind that a superficial growth may become deep-seated and pursue a rapidly fatal course, as in the galloping or phagedenic epithelioma described by Besnier.

Treatment.—Early and complete extirpation with the knife is the only method of treatment that should be employed in cancer of the mucous membrane of the mouth or of the lip.

On other parts of the body, as the neck, scrotum, etc., when the skin is freely movable and union by first intention can be secured, an excision offers the most rapid, painless, and satisfactory method of cure. If the operation is resorted to before the lymph nodes are invaded and if the incisions are made at a sufficient distance from the morbid growth, a cure may be looked for in the majority of cases.

Associated lymph nodes when invaded should be removed in as thorough a manner as possible.

Partial removal of cancer of the skin, even the most superficial, by the knife, curette, or caustics, accomplishes no good result and frequently stimulates these new growths to increased activity.

Superficial cancers of the skin are sometimes so situated that a cutting operation is followed by more deformity than after the employment of curettage and caustics. Many patients are so prejudiced against any cutting operation that they will endure the more prolonged and painful action of caustics rather than submit to the use of the knife. Under these circumstances the diseased tissue may be scraped away with the dermal curette and some suitable caustic applied to the resulting ulcer.

Numerous cures of cancer of the face have been obtained in this way by the writer, the caustics employed, as a rule, having been arsenic, in the form of Marsden's or Bougard's paste, or pure chloride of zinc. Arsenic is perhaps the best of all caustics as it is more certain in its action and presumably has a selective action on the morbid tissue. Marsden's paste is made by mixing two parts of arsenous acid with one part of powdered gum acacia and sufficient water to make the mixture of a firm consistence.

Robinson, who has devoted much time and consideration to the use of caustics in the treatment of cancer, prefers to vary the strength and duration of the application according to the cancer to be treated. He uses the paste in the strength recommended by Marsden and somewhat weaker, but never uses less than equal parts of arsenic and gum acacia. The paste is applied somewhat beyond the diseased area and is left on for from eight to twenty hours (Robinson). If the desired destruction of tissue is not obtained within the shorter limit a second but weaker application should at once be made until the necessary necrosis is accomplished.

The advantages claimed for the caustic treatment of cancer are the lesser degree of deformity which results and the greater certainty of reaching foci of diseased cells in the lymph vessels outside of the parent growth. It is, however, painful, and the separation of the resulting slough is somewhat slow.

Pain during the action of the caustic may be controlled by morphine, and the after-treatment should be conducted on the usual lines.

Before scraping away the morbid tissue as preliminary to the use of the caustic agent, the parts may be rendered anesthetic by a spray of chloride of ethyl. If this is followed by the application of tampons saturated in a five- or ten-per-cent. solution of cocaine the slight surgical procedure may be rendered absolutely painless.

Instead of employing destructive chemical caustics, like arsenic and chloride of zinc, the Paquelin or galvanocautery may be used to complete the treatment. The actual cautery is, however, not so certain to reach all the diseased cells as is the arsenical paste.

Of late years the writer has largely used acid nitrate of mercury instead of the preparations of arsenic and chloride of zinc. The epithelioma is first curetted under local anesthesia and afterward a sixty per cent. solution of acid nitrate of mercury is applied to the raw surface. This forms a superficial slough which requires from a week to ten days to separate. The ulcer remaining after the separation of the slough is treated with aristol under which it usually readily heals. Should any recurrence of the lesion take place the same procedure is repeated.

Patients who have been operated on for cancer should remain under observation for one or two years or longer, and the slightest recurrence should immediately be removed.

Radiotherapy.—This aspect of treatment is for obvious reasons best considered in connection with radiotherapy in general. If the use of *x*-rays is decided upon for the treatment of epithelioma better results are obtained by the single or massive dose method where the amount of the rays can be carefully measured.

Radium has given the best results in epithelioma of the edge of the lid, for here it is important to avoid scarring on account of the resulting deformity. In the early stages of these epitheliomata the application of radium is followed by disappearance of the growth with very little cicatricial formation.

JOHN A. FORDYCE.

Cardamom.—CARDAMOMUM. In the U. S. Pharmacopœia of 1890, this drug was defined as the dried, nearly ripe fruit of *Elettaria repens* (Sonnerat) Baillon (fam. *Zingiberaceæ*). In the present edition it is defined as the ripe seeds of the same plant, although the name is given incorrectly as *E. cardamomum.* White et Maton. The cardamom plant is a tall, reed-like, perennial herb, from six to twelve feet high. The flowers and fruits are borne upon special short, scaly stems, partly prostrate among the bases of the leafy culms.

The plant is a native of southern India, where also it has been long in cultivation. It has been introduced into other tropical countries. The cardamoms of commerce are mostly the product of cultivated plants, which are grown in the moist shade, either in clearings of the natural forests or in plantations of betel palms. The fruits are gathered before they are quite ripe. They are thoroughly washed, partly with soap and partly with a solution of a saponaceous fruit, and then bleached for some hours. They are frequently rubbed between the hands with a mixture of starch and buttermilk. The best are, however, the so-called "green cardamoms," simply dried in the sun, and of a pale greenish-brown color. They are ovoid or oblong, pointed, rounded-triangular, three-valved, and three-celled capsules. The husk, when dried, is of a pale yellowish-gray or brown, flexible, and tough. Those which have been starched have a white and almost chalky surface. The seeds, five or six in each cell, are irregularly compressed, brown, and spicy. The fruits of the best varieties are usually short, about once and a half or twice as long as broad (1 to 1.5 cm. = $\frac{4}{10}$ to $\frac{6}{10}$ in.), very plump and full. They are commercially called "shorts." Others, longer and more angular, are denominated "short-longs" and "longs." The larger and longer cardamoms are mostly the produce of other species of *Elettaria*, and are therefore unofficial. Their odor and taste are not so pleasant. In selecting cardamoms, the point of chief importance is to see that they are short, plump, and well-filled, as otherwise the proportion of husk is too great, and the strength is thus weakened through the diminution of he active portion. This difficulty can be avoided by specifying the amount of the seeds instead of the fruits. The seeds should constitute about seventy per cent. of the weight. The seeds from unfilled fruits are themselves defective, however.

FIG. 1213.—Malabar Cardamom. (Natural size.)

Cardamoms are also distinguished, according to the countries or ports from which they are exported, as Malabar, Aleppo, Madras, etc. The former are the most esteemed.

The shelled seeds are often imported. They are about one-sixth inch long and more than half as broad and thick, of a pale reddish-gray, strongly tuberculate and heavily grooved on one side. A spurious seed often intermixed is shorter, more angular, much darker and minutely papillose. Its taste is more bitter, and slightly camphoraceous.

The seeds contain about five per cent. of a pale yellow aromatic oil, of complex composition, which represents them in odor and taste. The ash of cardamom is rich in manganese. Cardamom is a typical aromatic, and is useful in all the conditions which call for articles of that class. As an agreeable flavor and appetizer, as a stimulant to digestion, and as a carminative in flatulence and in simple colic, it is sometimes, but not often, given alone. In combinations, as a pleasant and useful adjuvant and corrective, it is in more frequent use, acting favorably with cathartics, bitter tonics, stimulants, etc. But the principal use of cardamom is as a condiment or household flavor, for which purpose, especially on the continent of Europe and in the East, it is extensively employed. It is also used in flavoring liqueurs, and in curry-powder, etc. It is less irritating than the spices proper, and more so than anise and the milder carminatives. The dose of cardamom as an aromatic by itself would be gr. viij. to xv. (0.5–1.0). There is a ten-per-cent. official tincture which represents it completely. The compound tincture contains two per cent. each of cardamom and cinnamon, one of caraway, five of glycerin, and one-half per cent. of cochineal, in diluted alcohol, and is given in doses of fl. ʒ ij.–iv. (8.0–16.0). It also enters into the aromatic powder and the aromatic fluid extract.

Oil of Cardamom.—This term is understood as applying to the volatile oil, and not to the ten per cent. of fixed oil which the seeds yield. It is yielded to the extent of five or six per cent. It is of a pale yellow color, highly aromatic, has a specific gravity of about 0.900 and a rotation of +13°. Its important constituent is *terpinene* ($C_{10}H_{16}$). Its properties are identical with those of cardamom. It is, however, chiefly used for flavoring, especially liqueurs.

Henry H. Rusby.

Carden, Henry Douglas.—Born in Worcester, England; date of birth not known. In 1838 he became one of the surgeons of the Worcester Infirmary, and he held the position up to 1861, when he resigned. He won for himself a place in the history of medicine by devising a mode of amputating the thigh which necessitates the employment of only one flap composed entirely of skin. In this operation the femur is sawed through the condyles just above the articular surface. His death occurred in 1872.

The title of the paper in which the operation referred to above is described is as follows: "On Amputation by a Single Flap," London, 1864. A. H. B.

Cardiac Murmurs.—In arriving at a diagnosis of any cardiac condition that may present itself one must employ the usual measures of physical diagnosis, palpation, percussion, and auscultation, as well as inspection. It would be extremely difficult to express an opinion as to which of these measures is the more important in heart diagnosis, but in any event it behooves one who would understand and intelligently appreciate the condition existing within the heart to become thoroughly familiar with all the auscultatory phenomena connected therewith.

The tones or sounds heard in the cardiac area may be divided into two distinct groups: (1) The normal heart tones; (2) the various pathological tones arising in this area, designated variously as murmurs, bruits, adventitious heart sounds, etc.

The Normal Heart Tones.—These are two distinct, usually clear-cut, positive, sounds that occur in connection with the normal functioning of the heart. They are spoken of as the first or *systolic* sound and the second or *diastolic* sound. The first sound is normally somewhat prolonged, low pitched, and rather dull. It is more or less booming in character, especially when compared with the snapping quality of the second sound. The second sound is sharper, shorter, and of a higher pitch than the first. These sounds are well simulated by a repetition of the words "lubb-dubb," placing the accent upon the last word. They are heard best in the mitral area, the region of the apex beat, which is normally in the sixth intercostal interspace to the left of the sternum in the nipple line. In some instances the apex beat is both visible and palpable, in others only palpable. The heart tones are heard very distinctly, however, over the entire cardiac area and in some instances of increased heart activity are heard at distances which surprise one.

Each of the heart tones or sounds is followed by a pause, which, in the normal heart, is quite distinct and definite; the one occurring at the end of diastole being decidedly the longer and occupying in the cardiac cycle a little more time than the two sounds combined.

The cause of the heart sounds has been a very fruitful source of discussion and many diverse views have been held and proclaimed. It can, though, be safely stated that they are due to two elements; the contraction of the heart muscles and the closure of the valves. The diastolic sound is undoubtedly purely of the valvular origin while the systolic is composed of both elements, muscular sound and valvular vibrations. The term, muscular sound, used in this connection is not to be confused with the term as applied to the skeletal muscles. In the skeletal muscles the sound depends upon the number of individual contractions which produce the tetanic condition, while the heart muscle contraction, on the contrary, is not tetanic. This muscle tone is probably caused by the vibrations being transmitted to the thorax while the rigidly contracted apex of the heart is held against the chest wall. The valvular element is the result of the sudden closing of the valves due to a lessened pressure behind plus an increased pressure in front. This results in more or less snapping together of the valve segments, thereby putting the chordæ tendineæ and the papillary muscles upon a stretch and setting up in these elements more muscular vibrations. Now dependent upon which of these elements, *i.e.* muscular or valvular, predominates in the first sound it will be either a low-pitched, dull, comparatively slow boom or a short, sharper, higher-pitched boom, but in no instance becoming as short, sharp, or high pitched as the second sound.

The second heart sound is the result solely of the closure of the pulmonic and aortic valves. It is therefore possessed of the character of a valve sound, being shorter, sharper, and higher pitched than the first and not partaking of a booming nature. There is no muscular element in the second sound. The two sounds are sometimes illustrated by using a linen handkerchief. In simulating the first sound the handkerchief is grasped by the corners and the edge suddenly drawn taut; the second sound is reproduced by using just one-half the border and manipulating as in the first instance.

As mentioned above, each of these sounds is followed by a distinct pause. These pauses are paired with the sound which they follow and are consequently preceded by the term systolic or diastolic as the case may be. The heart cycle is, then, divisable in this manner: *First sound* plus *first or short pause* equals systole; *second sound* plus *second or long pause* equals diastole. In a normal heart the beats and pauses follow each other with a regular sequence and each occupies a definite amount of time in the cardiac cycle. It may be readily seen in the diagram (Fig. 1214). It will be noted that the pause following diastole is at the end of the cycle.

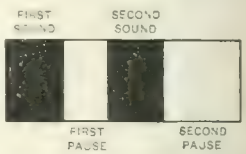


Fig. 1214.—Diagram Showing the Sequence of Heart Sounds and Pauses.

The systolic tone is best heard at the apex and over the tricuspid valve. The diastolic tone being accentuated over the great vessels, aorta and pulmonary artery. The apex beat, it may be mentioned here, is systolic in time. The reason we hear only two sounds upon auscultating the heart is due to the fact that normally all the muscles and valves of the heart act only in systole or diastole. When an extra systole occurs, as is sometimes the case, three distinct sounds are then heard. There are certain variations and irregularities in the cardiac rhythm that may be noted in this connection.

Embryocardia.—This is a condition seen when, from causes that weaken the walls of the heart, there occurs a distinct shortening of the diastolic rest space and the cardiac sounds follow each other with a watch-like regularity. It is often designated the "tick-tack" heart from its resemblance to the ticking of a watch. It impresses one as very similar to a fetal heart beat. The pause following the first sound is likewise affected at times, particularly in certain failures of compensation. In this case it is due to an incomplete contraction of the ventricle.

Reduplication or doubling of the heart sounds also occurs. It is heard most frequently in aortic regurgitation and is due to any factor that causes an increased peripheral pressure. An increased pressure

in the pulmonic circulation will likewise cause at times a reduplication to the pulmonic second sound.

The Gallop rhythm is heard as the result of reduplication added to a shortening of the diastolic pause. In this condition one can hear at the apex three distinct sounds following each other in such rhythm as to suggest the hoofbeats of a galloping horse. Then there are four conditions that are usually mentioned together in any discussion of heart sounds; tachycardia, bradycardia, arrhythmia, and palpitation.

Tachycardia and *palpitation* are both a very much quickened heart impulse. The pulse becoming very rapid. The differentiation usually made is that a tachycardia is imperceptible to the patient while a palpitation is always perceptible. In fact, so much so, as to be in some instances alarming to the patient. It is a frequent manifestation of the various neuroses.

Bradycardia is a condition in which the heart impulses are markedly slowed. In some instances the pulse falling as low as forty or fifty beats per minute. There are many cases both of tachycardia and bradycardia perfectly compatible with health, that is, are found as a normal condition in people who, so far as can be ascertained, are perfectly healthy.

Arrhythmia is a condition of irregularity in the force or rhythm of the heart beat and when present in a slight degree may be physiological. However, when very marked or constant it constitutes an abnormal condition. It arises in the course of certain diseases and is due to different causes. These matters will be discussed more fully later when individual lesions are considered.

Adventitious Sounds, Murmurs, or Bruits. Personally, I prefer the term murmur which I usually qualify with the addition of the term cardiac, respiratory, friction, etc., as the case may be.

These murmurs are classed in two groups:

(1) *Organic* murmurs, sometimes designated *valvular* or *true;* (2) *Inorganic* murmurs, also called *functional* or *accidental.*

The terms true and accidental are, to my mind, rather vague when used in this connection, for an accidental murmur, if a murmur at all, must necessarily be a true murmur. So I would discard them. The term functional is likewise open to some objection. Any murmur which may occur is truly speaking a functional murmur in that it is directly dependent upon the functioning of the heart in being elicited. However, this may probably be drawing too fine a distinction and the term has, through usage, been adopted to refer to what will be described below as an inorganic murmur. The terms expressing most clearly one's meaning and less liable to be confounded are the terms organic and inorganic; organic referring to those murmurs which are the result of definite anatomical changes in the heart musculature or valves; and inorganic referring to the class of murmurs not dependent upon an anatomical change and whose causation will be discussed later.

Organic Murmurs.—These murmurs result from anatomical changes that allow the blood to flow in a reverse direction after having been forced onward—regurgitation or insufficiency; from a narrowing of the valvular orifices or a roughening and thus impeding the normal onward flow of the blood—stenosis or obstruction. These conditions give rise to murmurs by furnishing the necessary conditions to set up eddies in the blood current. The accompanying illustration shows very well the mechanics involved. If we take a glass tube and dilate it in the middle so that it shows a pouch (Fig. 1215) and allow a stream of water to flow in the direction indicated by the arrow there will be eddies set up in the current as shown by the small curves. Fig. 1215 shows the mechanics of regurgitation. Fig. 1216, stenosis, and Fig. 1217, roughened valves, which is in reality a stenosis also.

Stenosis or obstruction is the result of an abnormal narrowing of the valvular orifice (in some instances to a mere slit) or to a roughening of the valves or a deposit upon the edges of the valve segments. This latter condition not only serves to impede the onward flow of the blood stream but also serves to embarrass the closure of the valves and thus enters as a factor in regurgitation.

Regurgitation or insufficiency is the effect of imperfect closure, from either valve changes or a dilated orifice, designated *absolute* and *relative* respectively. By some writers a separate distinction is given to the

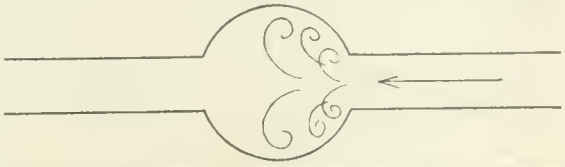


Fig. 1215.—Diagram to Illustrate the Production of a Cardiac Murmur Through Regurgitation from the Aorta or in an Aneurysmal Sac. The arrow shows the direction of the blood current and the curled lines the audible blood eddies. (From Cabot's Physical Diagnosis, Wm. Wood & Co.)

changes produced at the aortic and pulmonic valves by an increased size in the vessels opening from these orifices. But an enlarged orifice is an enlarged orifice and so produces a regurgitation whether it is caused by a distinct, definite dilatation of the orifice itself or is pulled open by the vessel leading away from the opening.

The *inorganic* or *functional* murmurs are those which may occur as stated, with no anatomical lesion or pathological change in the heart presenting

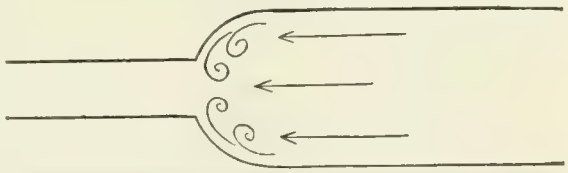


Fig. 1216.—Diagram to Illustrate the Production of a Cardiac Murmur Through Stenosis of a Valve-orifice. (From Cabot's Physical Diagnosis, Wm. Wood & Co.)

itself. They are due to two causes: (1) certain blood changes, and (2) an increase in the rapidity and force of the heart beat; the first occurring especially in severe anemias where the blood is markedly altered, the specific gravity being lowered. The murmur is often spoken of as an anemic or hemic murmur. In the second instance the murmurs result from the vibrations set up at the valve openings by the excessively rapid action of the heart or an increased force of the individual contractions. These murmurs are more

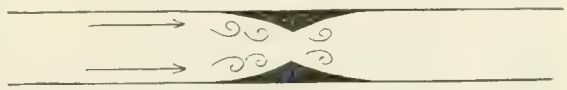


Fig. 1217.—Diagram to Illustrate the Production of Cardiac Murmurs Through Roughening of a Valve. (From Cabot's Physical Diagnosis, Wm. Wood & Co.)

affected by exercise, position, and respiration than are the organic murmurs.

They are almost always systolic and are never musical in quality. They are heard over a limited area and are *not* transmitted away from heart.

The *organic murmurs* are very diverse in character. They are more or less prolonged noises and thus contrast very sharply with the normal heart tones which are, as stated, brief, the sound being sharply defined. Endocardial murmurs are both systolic and diastolic in time of occurrence, dependent upon the situation

and the nature of the causative lesion. They are short in some instances, prolonged in others. They are heard best in different areas depending upon the valve from which they arise and are transmitted in a definite direction and over a definite area. They have a point of maximum intensity, and this is sometimes transmitted from the place at which the murmur actually arises to another point. The murmurs are transmitted toward the axilla, upward toward the neck, down the sternum, or through the thorax, differently caused murmurs choosing different routes. In character they are generally *blowing* or *puffing*. They may be *rough* or *scraping* in nature; at times, *musical, whistling* or *singing; intense* or *distant; harsh* or *soft; prolonged* or *short; crescendo* or *diminuendo, i.e.* crescendo beginning gradually and ending sharply; diminuendo beginning sharply and ending gradually;

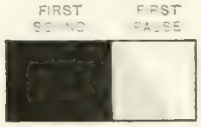


FIG. 1218.—Systolic Murmur.

FIG. 1219.—Late Systolic Murmur.

or a combination of the two, beginning gradually and fading away gradually, or beginning sharply and ending sharply. In some instances these murmurs are very difficult to elicit and in others are so prominent as to be heard some distance away.

The most important points to be held in mind regarding murmurs are: (1) Time of occurrence (presystolic, systolic, late systolic, diastolic). (2) Point of maximum intensity. (3) Direction and area of transmission. (4) Effects, upon murmur, of exertion, respiration, and position. (5) Intensity, quality, and duration.

1. *Time of Occurrence.*—This is with relation to the time occupied in the cardiac cycle. The cardiac cycle, as before stated, consists of the two heart sounds and two pauses. A murmur is designated *systolic* that replaces the first sound of the heart or arises at

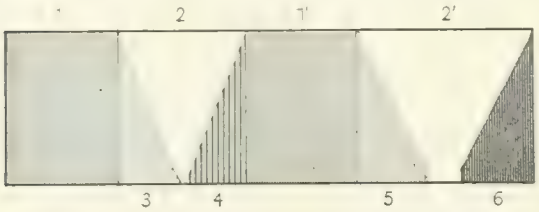


FIG. 1219.—1 and 1', Heart Sounds; 2 and 2', Rest Periods or Pauses; 3, Systolic Murmur; 4, Late Systolic Murmur; 5, Diastolic Murmur; 6, Presystolic Murmur.

the end of the first sound or coincident with the first sound and occupies all or a part of the first pause. A murmur arising in the pause after the conclusion of the first sound is a *late systolic* murmur. These murmurs are represented in Figs. 1218 and 1219. A murmur replacing the second sound, arising during the second sound or immediately thereafter is known as a diastolic murmur. The murmurs arising late in the diastolic pause are called *presystolic.*

The only accurate manner in which to judge the time of a murmur is, at the moment of auscultation, to palpate the apex beat or carotid pulse. The apex beat is, as already noted, systolic in time. Comparison with the carotid, however, is not as definitely accurate as the apex comparison. The radial pulse is markedly less reliable than the carotid. In a rapid heart Landis gives the delay in a radial pulse at 0.22 of a second and thus in this instance the radial pulse would become more nearly diastolic than systolic. A murmur is regulated in time by the nature of the lesion and the valve at which it occurs. For instance, a mitral regurgitant murmur is systolic in time while a mitral stenosis is diastolic. The following grouping is an aid to remembering the time of murmurs at the different valves:

	Systolic	*Diastolic*
Regurgitation	Mitral	Aortic
	Tricuspid	Pulmonary
Stenosis	Aortic	Mitral
	Pulmonary	Tricuspid

2. *Point of Maximum Intensity.*—The practical import of this is, like the preceding, one of diagnostic differentiation. The different lesions at the different valves are transmitted to parts other than those at which they arise and it at times is difficult to say just where a murmur arises if we do not have the point of maximum intensity to guide us. Each murmur has an individual point at which it can be heard and studied best. This point is designated the point of maximum intensity. It will be discussed again in dealing with the separate valve lesions.

3. *Direction and Area of Transmission.*—As just mentioned each valve transmits its murmurs along definite lines and toward a definite area. This fact has been proven by clinical experience and borne out by postmortem findings, and is very helpful in enabling one to decide whether he is dealing with one lesion or multiple lesions that happen to be synchronous. In lesions of this nature the points of maximum intensity are also a great aid. The area and the direction of transmission will also be considered when discussing the individual valvular disturbances.

4. *Effects of Exercise, Respiration, and Posture.*—Different postures will elicit murmurs otherwise inaudible. For example Dr. Heinrich Stern has found that a tricuspid murmur which cannot be detected in the erect or recumbent position will be distinctly brought out by placing the patient in a position with the head lower than the body. On the other hand murmurs readily audible while the patient is standing or sitting may disappear upon reclining, notably a presystolic murmur. Diastolic murmurs, as a rule, are not as much affected by posture as systolic. Exercise has a tendency to increase the intensity of a murmur; thus it will bring out a feeble murmur or a frank murmur will be intensified. Aside from its diagnostic help, exercise is also of prognostic aid. A murmur becoming decidedly more intense, harsh, or prolonged after moderate exercise (brisk walk up and down room several times, sitting-up exercises, etc.) would point toward a rather severe lesion, and one that showed a weakening after exercise would argue for a weak heart.

The chief interest in respiration as it affects heart murmurs is the behavior manifested by organic murmurs on one hand and inorganic on the other. Organic murmurs are usually heard best at the end of expiration, becoming less distinct as inspiration advances and the expanding lung covers the heart. Inorganic or functional murmurs are to be heard best, chiefly at the end of inspiration. The respiratory murmur known as the cardiorespiratory will be discussed below in connection with murmurs heard in the precordial area not dependent upon the heart.

5. *Intensity, Quality, and Duration.*—The intensity of heart murmurs, as with normal heart tones, is of course relative and depends upon conditions without the heart as well as upon conditions within the heart. In corpulent men with fat chest walls and in women with well-developed breasts the sounds emanating from the heart would of course be less distinct than in a poorly nourished individual. Edema of the chest wall, emphysema, etc., all play a part and these must be considered in any given case, if present. The intensity of a murmur is of note as to its behavior under

given conditions. To illustrate: a strong, loud murmur is indicative of a forceful beat arising from a strong heart, and should a murmur of this nature weaken it usually points toward a weakening of the heart and is to be regarded seriously. When one is definitely sure of a valve lesion and compensation remains good an increase in intensity usually means progressive advance in the lesion. On the other hand, in a heart so weakened that the murmur may have disappeared an increased intensity is to be regarded as a good sign. So, conclusions to be drawn from the intensity of a murmur are to be interpreted with an allowance for the influences affecting the murmur and all the circumstances connected with the case upon which one may be fortunate enough to obtain information.

Quality.—The usual murmur is *blowing* in quality, somewhat similar to the letter "F" whispered. They may be *high pitched* or *low pitched*, in the former approaching the sound of a whistle at times, and may become *musical* murmurs whose pitch can be definitely identified. A *rasping* murmur is low, and has a distinct tearing sound. The *presystolic roll* is, as its name implies, a murmur heard just before systole and described by Cabot as "rumbling or blubbering and maybe remind one of a short drum roll."

Duration.—Little aid can be derived from the duration of a murmur. It may be of any length, occupy the whole of systole, of a diastole, or a part of either. A short diastolic murmur usually is of serious import.

In addition to the murmurs found in and resulting from the heart directly, there are other varieties to which it is well to direct attention in this connection.

The Arterial Murmurs.—These are either systolic or diastolic, and in the case of systolic murmurs are usually heard in the vessels near the heart and are the result of murmurs produced either in the heart or aorta and transmitted. They may, however, arise at or near the point at which they are heard and are in this instance due either to pressure, to dilatation of artery, to a roughened internal coat, or to blood changes (anemia). Pressure murmurs may be readily produced by the stethoscope: the aneurysmal bruit is an example of the dilatation etiology. Diastolic murmurs are heard in cases of severe aortic regurgitation. They have been reported in the femoral artery as a double murmur in pregnancy, lead poisoning, and mitral stenosis.

Venous Hum.—This is a normal sound heard with greatest intensity in the jugulars and best in the right just above the clavicle. This murmur disappears as middle age is reached. It is a continuous low hum loudest at the time of auricular diastole and during inspiration. It is affected by posture; in some cases disappearing upon reclining. Anemia intensifies this murmur.

Arterial Varix (communication of artery and vein direct).—In this condition a systolic murmur is heard over the entire area involved.

Cardiorespiratory Murmur.—This is a murmur heard over the apex of the heart and along the left heart border. It has no special diagnostic value. It is *not* transmitted as are the cardiac murmurs heard in this same locality. This murmur is the result of the compression of part of the lung overlying the heart and between the heart and chest wall. The compression forces the air out of the alveoli with a fine blowing sound or, when the air cells and bronchioles contain secretions, with fine crackling râles. While caused by the contraction of the left heart, the sound is not absolute in time of occurrence with the heart's action. It is heard during systole and after diastole. The intensity is increased or decreased by the respiratory rate and depth and the posture. In each instance in which it is heard the murmur will probably behave differently, in one case being intensified by inspiration and in another by expiration. It may be intensified by firm pressure of the stethoscope. In addition there are heard in this area the *pericardial* sounds and the *pleuropericardial* sounds. These are not cardiac murmurs and will therefore be discussed elsewhere. Suffice it to say the pericardial sound is rough, grating, and irregular. It is a friction sound rather than a murmur. It does not occur with systole or diastole but overlaps the sounds and comes into the pauses. The pleuropericardial sound is the sound resulting from inflamed pleural surfaces grating against each other. In sound they are practically indistinguishable from pericardial friction sounds. A differentiation between pericardial sounds and endocardial murmurs can usually be made by remembering that the pericardial sounds do not correspond either with systole or diastole and do not constantly occupy any definite portion of either period. Endocardial murmurs are deeper seated, *i.e.* in auscultating one does not receive the impression of superficialness experienced in pericardial rubs. Pressure with the stethoscope does not affect cardiac murmurs but often increases the intensity of a pericardial sound. The cardiac murmurs are more regular and do not vary as do the pericardial sounds.

Houston B. Hiatt.

Cardiac Therapeutics, General.—See *Heat, Functional Disorders and General Therapeutics of.*

Cardiography.—Broadly speaking this term (from καρδία, the heart, + γράφειν, to write) is used to designate the art of recording graphically the movements, sounds, and differences in electrical potential of the several parts of the heart, the movements of the blood-vessels (arteries and veins) and other organs (liver, etc.) influenced by heart action.

Description of Apparatus.—The *sphygmograph* (σφυγμός, the pulse, + γράφειν, to write) was the instrument first devised to record graphically circula-

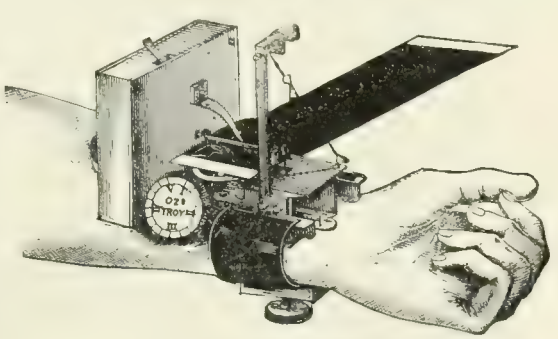


Fig. 1220.—Dudgeon's Sphygmograph.

tory phenomena. It records the movements of the pulse. The *polygraph* (πολύς, many + γράφειν, to write) is somewhat more elaborate than the sphygmograph and is used to record simultaneously the movements of two or more organs (heart, arteries, veins, lungs, liver, etc.) The ingenuity of numerous inventors during the last fifty years has afforded us many kinds of apparatus but a description of a few types will serve to illustrate the main principles and their use. Essentially each instrument consists of a recording surface moved by means of clock-work, and a writing lever, the recording paper may be plain white paper (Mackenzie, Marey, etc.) or smoked paper (Dudgeon, Jacquet, Marey, Uskoff, etc.), the writing lever may be a delicate wire which scratches the smoked paper (Dudgeon, Jacquet, Uskoff, etc.) or may carry an ink pen (Mackenzie, Marey, etc.).

Some instruments are made to be fastened on the wrist and applied directly to the pulse (Dudgeon, Marey, Jacquet), others (Mackenzie, Uskoff) are arranged to be placed on a table near the patient and the movements of the organs to be recorded are conveyed to the writing levers by air pressure through rubber tubing connected with specially adapted tambours. Most of the instruments are provided with a time marker which records fifths or tenths of a second.

Dudgeon's sphygmograph is applied to the wrist in such a manner that a spring on its under surface is brought in contact with the radial artery. The pressure of this spring on the artery is regulated by the tightness of the band which holds it in place, a further adjustment can be made by means of a small wheel connected with a cam. The movements of the artery are transmitted by the spring to the writing pen by means of a series of levers and are recorded on a strip of smoked paper moved by clock work. The Dudgeon is a simple and satisfactory instrument for recording the movements of the pulse. A few years ago Mackenzie modified the Dudgeon by attaching to it an additional writing lever with a connecting tambour making it serviceable as a polygraph.

Jacquet's sphygmocardiograph is a beautifully constructed polygraph which is provided with two independent clock mechanisms, one to move the smoked paper (with fast and slow speed adjustments), the other to record the time intervals. It is built to be applied to the wrist, the movements of the artery being transmitted directly by means of a spring and levers to a delicate writing point. In addition to these means for recording the pulse and time intervals one or two other writing points connected with tambours are provided to record simultaneously other movements, such as the apex beat, jugular pulse, etc.

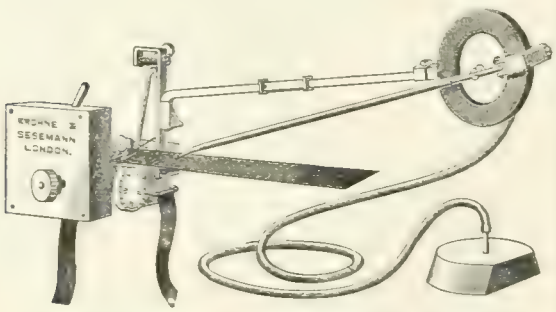


Fig. 1221. Clinical Polygraph. (Dudgeon-Mackenzie.)

These latter movements are taken up by suitably contrived apparatus, cups, etc., and are transmitted to the tambours attached to the writing levers by means of air pressure in rubber tubing. The writing points are kept in contact with the smoked paper by the force of gravity, a considerable aid to the operator since it permits him to direct his attention to the other features of the manipulation.

Uskoff's sphygmotonograph is provided with four writing levers which are kept in contact with the strip of smoked paper by the action of gravity. The pulsations of the brachial artery are taken up by a cuff similar to that used for blood pressure determinations and are transmitted to a rubber ball enclosed in a glass bulb, the interior of this bulb is connected with a tambour to which is attached a writing lever.

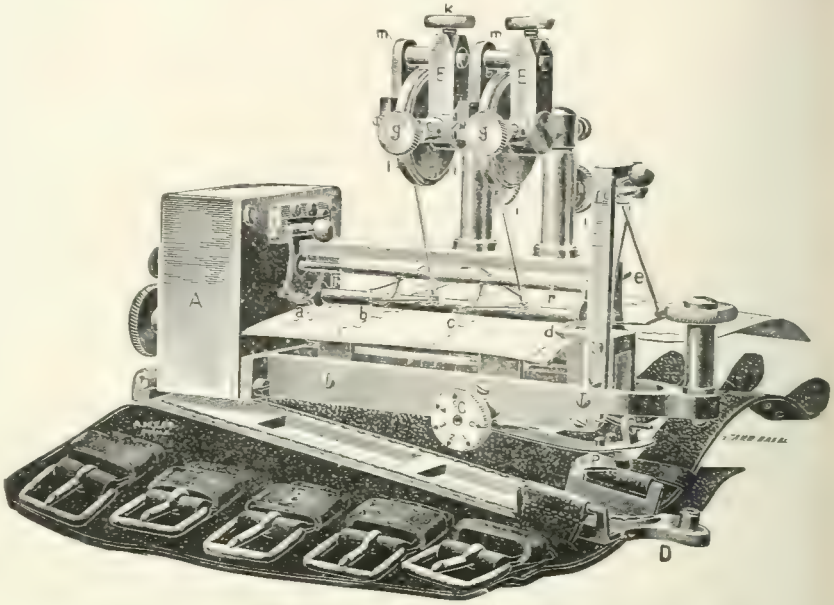


Fig. 1222. Jacquet's Sphygmocardiograph. (Arthur H. Thomas Company.)

This system is connected by means of a three-way cock with a column of mercury whose height may be recorded by an ingenious blowing device acting on another writing lever. A third tambour with its writing lever may be used to record the movements of the veins, apex, liver, or respiration, which are received by air transmission through rubber tubing from a cup or other device applied to one of these organs. A fourth writing lever records fifths of a second. The paper and time marker are moved by separate clock mechanisms. The more recent models are provided with two speeds for moving the smoked paper and a special support for a long roll of ready smoked paper which may be procured with the instrument. This is an exceedingly satisfactory instrument for ordinary routine polygraph work, the adjustment of the brachial cuff is quickly made and usually takes much less time and attention than is required by the instruments attached to the wrist. The attachment for recording the various pressures I have found of little value, but the height of the mercurial column may be read directly during the adjustment of the brachial cuff and this affords a simple means of determining blood pressure while one is preparing to take a graphic record of the pulse. In adjusting the cuff for recording the brachial artery the pressure is usually raised to a point which is the equivalent of diastolic pressure as this gives the greatest excursion to the writing point.

Mackenzie's ink polygraph is shown in Fig. 1224. It has the great advantage over other instruments of writing in ink on a strip of paper furnished from a roll. By means of th s instrument a long-continued record may be taken, often an important feature when irregularities occur at infrequent intervals. The paper and time marker are driven by separate clock mechanisms and the movements of the blood-vessels are magnified by the length of the writing

levers. The speed at which the paper moves may be regulated at will. The use of ink does away with the necessity of smoking the paper and fixing the tracings with varnish.

Hospital Polygraph.—For hospital work we have found useful a large Ludwig kymograph mounted on a table which can be wheeled to the bedside. The smoked paper can be used on a single drum as shown in the cut or a double drum may be arranged to carry a strip of paper fifteen feet long. The drums may be made to move at any desired velocity. The time marker is activated by a dry-cell battery and by adjusting the length of the steel rod of the device for making and breaking the current (4, Fig. 1225), any desired time interval, from 0.2 to 0.02 second, may be recorded. For obtaining accurate and elaborate records we have found this apparatus very satisfactory.

Accessory Apparatus for Polygraph Work.—There are certain pieces of apparatus, which, while not essential for the ordinary polygraph work, are helpful and often materially facilitate the taking of records. Among those which have been found useful are the following: *arm rest* which may be attached to the patient's forearm, with a handle which is

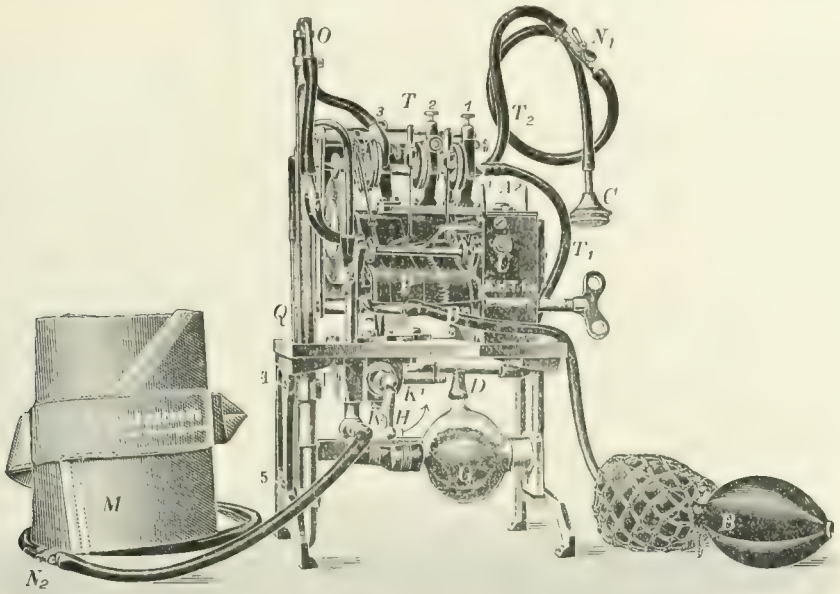


Fig. 1223.—Uskoff's Sphygmotonograph (Arthur H. Thomas Company)

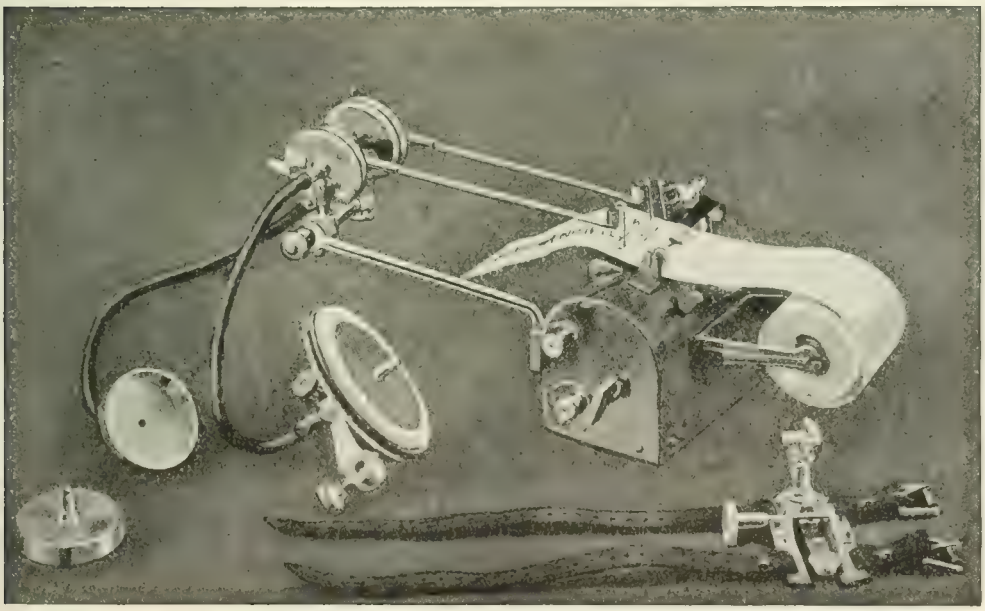


Fig. 1224.—Mackenzie's Ink Polygraph. (Arthur H. Thomas Company.)

received in the palm of the hand; suitable adjustments permit of the desired degree of extension of the wrist so that the radial artery is more readily brought and held in contact with the receiving apparatus of the various instruments attached to the wrist. In Fig. 1225 are shown (1) a metal *wheel for smoking paper;* (2) a convenient form of *basin for varnishing*

(6) *pneumograph* to facilitate the recording of respiratory phenomena.

The Micrograph.—This instrument, devised by Albert C. Crehore, Ph.D., contains a thin metal diaphragm similar to that of a telephone, on one side of which there is an air chamber connected by a tube to a tambour receiver located on any desired portion

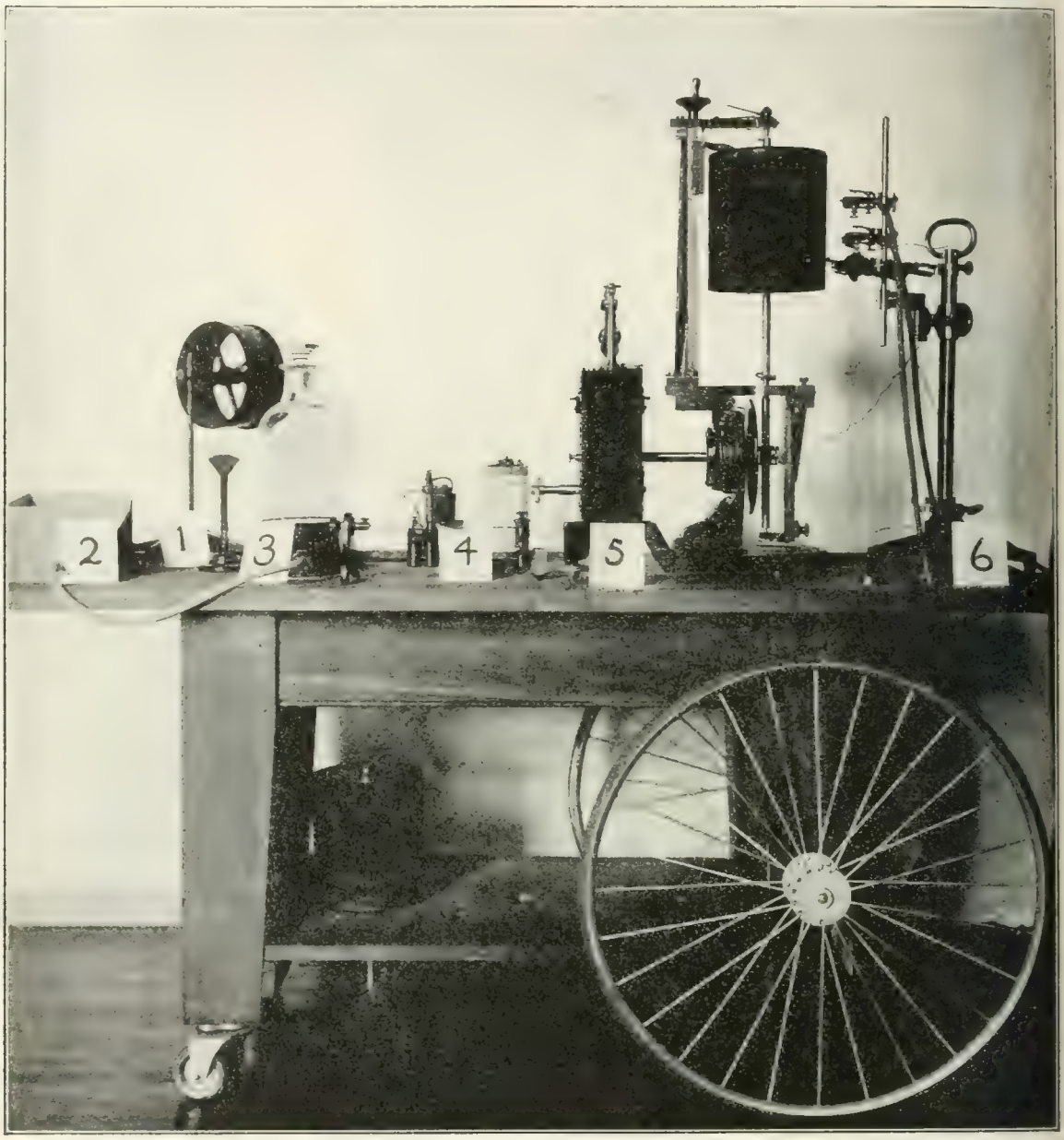


Fig. 1225.—Hospital Polygraph.

tracings, and (3) connected with this by tubing a *receptacle for holding the varnish* when not in use; (4) adjustable *apparatus for making and breaking the electric current* in connection with a time recorder. In Fig. 1226 are shown (1) various forms of *cups* and *receiving apparatus,* (2) *receiver for brachial artery,* (3) *for apex,* (4) *for radial,* (5) *Jacquet's chronograph* and

of the body. The diaphragm is free to respond to all vibrations transmitted to it through the medium of the confined air column. The movements of the diaphragm are made visible by employing the phenomena of the interference of light. To the surface of the diaphragm D (Fig. 1227) is attached a plane mirror E polished on its upper surface to make a metal

reflector. Just above this is placed a plano-convex lens L, with the plane surface parallel to but not touching the surface of the mirror. A mercury vapor lamp is placed above the instrument and brings to the view of the observer a series of interference bands of light between the two reflecting surfaces. As the diaphragm moves, the reflecting surface E approaches and recedes from the lens L, the concentric circular interference bands contract and expand respectively. By this means the movements of the diaphram are magnified about 50,000 times. The interference bands may be recorded on a moving photographic plate (Fig. 1228). From this negative a "pressure-time" curve can be accurately constructed by measuring the distance on the plate of the appearance and disappearance of the interference bands and plotting these measurements (Fig. 1229). By using several instruments simultaneously and projecting their images on one plate, synchronous curves of various physiological events may be recorded. The instrument is exceedingly delicate and responds to waves of sound as well as to those of motion. It is far more delicate than the polygraph instruments which make use of writing levers and avoids the errors of "inertia" and "fling" which are inherent in the lever instrument.

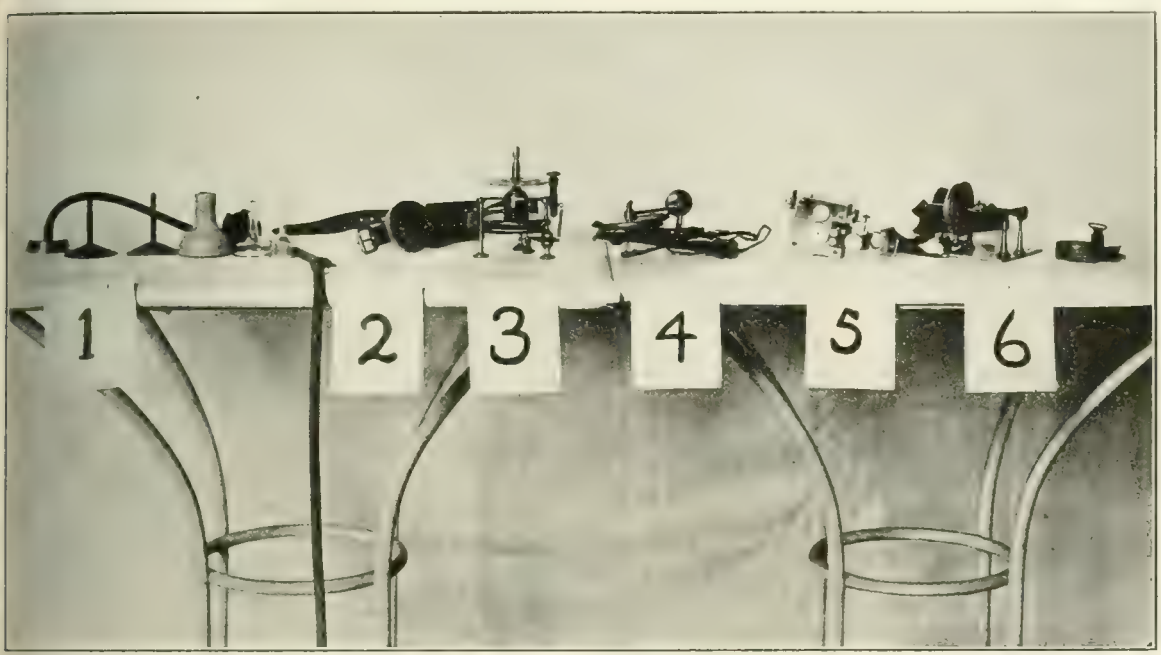


Fig. 1226.—Accessory Apparatus for Polygraph Work. 1, Receiving cups; 2, receivers for brachial or carotid artery; 3, for apex; 4, for radial; 5, Jacquet's chronograph; 6, pneumograph.

Phonocardiography (*φωνή*, a sound; *καρδία*, the heart, + *γράφειν*, to write) is the art of recording graphically the sounds of the heart.

Francke's capsule offers one of the simplest methods. The sounds of the heart are taken up by a cup fastened to the precordium and are transmitted by rubber tubing to the "capsule," which consists of a cylindrical metal tube slightly flattened on one side at the distal end; this end is covered by a delicate gutta percha membrane upon one side of which is mounted a light quadrilateral piece of gelatin which serves as a support for a small oscillographic mirror. The mirror is illuminated by the rays from a Nernst lamp and its movements are recorded photographically. Mechanical pressure effects are excluded by means of a lateral opening in the tube so that only those vibrations which are due to sound waves are recorded.

The phonoscope of Weiss (Fig. 1230) is so constructed that the sounds of the heart are received on a soap bubble, a membrane which is said to exceed in delicacy the most sensitive microphone yet devised, the oscillations of this membrane are transmitted to a delicate filament of silvered glass, bent at a right angle and placed in the center of the soap bubble. The movements of this glass rod are recorded by photographic apparatus. By means of this instrument the normal sounds of the heart and murmurs may be recorded.

The Gerhartz apparatus receives the sound waves on a membrane of collodion, the movements of this membrane are transmitted by a delicate needle to a minute iron disc resting between the poles of a small magnet which acts as a delicate means of damping the movements of the membrane to the desired degree. To one side of the disc is attached an oscillographic mirror which reflects the rays from a small electric light to the photographic film. By proper adjustments this instrument may be used to record pressure and sound waves or sound waves alone (Fig. 1232).

Other methods of recording heart sounds and murmurs are, the use of a microphone in connection with the string galvanometer of Einthoven (Fig. 1233), and the micrograph of Crehore (see Micrograph).

Practical Points in Taking Polygraph Records.—Much time and annoyance in taking polygrams may be saved if one systematically pays attention to the following apparently insignificant details. One should always first examine his instrument to see if all parts, particularly the tambours, are in good working order; the clock work (usually two sets) should be wound. If smoked paper is to be used an ample supply should be prepared so that one need not interrupt his work for this purpose during the record-taking period. For smoking the paper a large candle, a kerosene lamp, burning camphor, or a gas burner fitted with a fantail may be employed.

Personally I prefer the gas burner when practical as by this means the smoke is laid on the paper more evenly and less heavily than by the other methods. If the ink polygraph is used the pens should be carefully cleaned and filled with the writing fluid.

The patient should be placed on a couch or bed with clothing loosened to allow access to the parts which it is wished to investigate, he should be in a comfortable position so that he may relax and lie

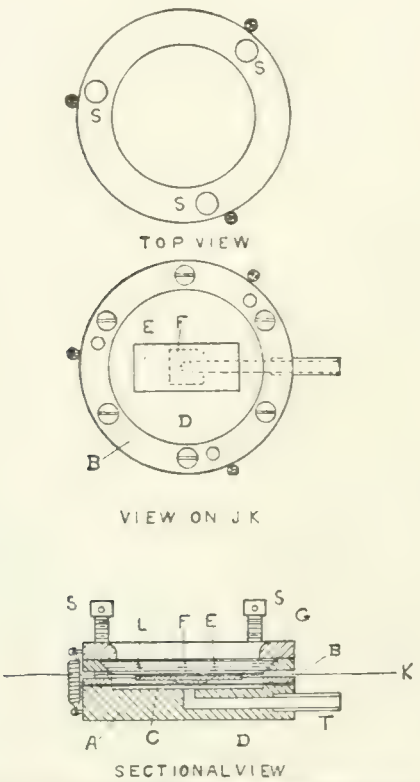


Fig. 1227.—The Micrograph. Crehore and Meara in the *Jour. Amer. Med. Ass'n.*)

quietly. In taking a record of the jugular pulse the shoulders should be slightly raised, the head somewhat flexed forward and rotated to the right and supported by pillows so that the sternocleidomastoid muscles may be perfectly relaxed. When a radial tracing is taken, the position of the radial artery should be marked with a skin pencil, this will be found to facilitate greatly the correct adjustment of the spring of the instrument over the radial artery.

Fig. 1228.—Micrograph Record

The spring of the instrument should rest immediately over the artery to avoid distortion of the form of the pulse tracing, which a lateral displacement may cause. If the pressure of the spring on the arterial wall is equivalent to the diastolic presssure of the patient the movements of the spring will be maximal, if this gives a movement to the writing lever greater than is desired the excursions may be reduced by slightly increasing or diminishing the pressure of the spring (in polygraph work the time relations of the various tracings are usually of greater importance than the size of the various waves). In adjusting the brachial cuff of the Uskoff or Erlanger apparatus, the pressure is usually raised to a point equivalent to the patient's

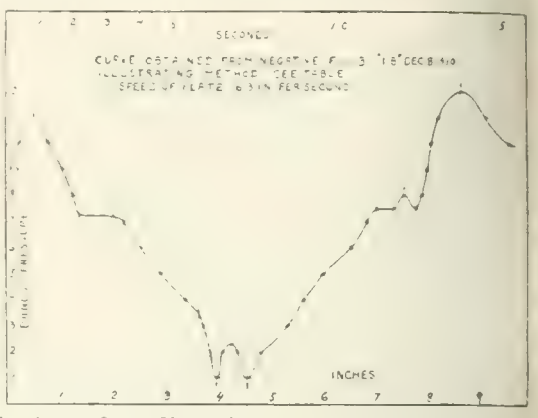


Fig. 1229.—Curve Obtained by Plotting the Micrograph Record (Crehore and Meara, *Jour. Amer. Med. Ass'n.*)

diastolic pressure (in using this instrument one sometimes meets with difficulty in securing a sharp "foot-point" for the waves of the brachial record). The receiving apparatus for an apex tracing may be a

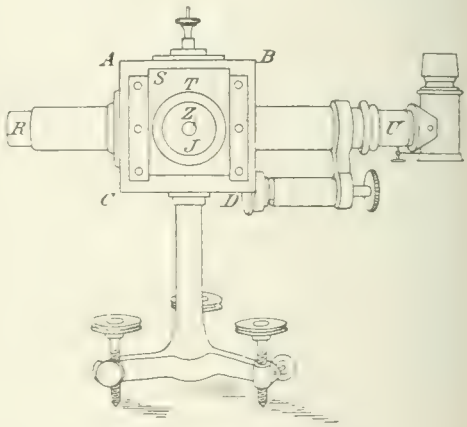


Fig. 1230.—Phonoscope of Weiss.

small Mackenzie cup or one of the more elaborate forms of the so-called "cardiographs," which may be strapped to the chest wall or held by an assistant. The position of the apex thrust should be marked

Fig. 1231.—Registration of the Heart Sounds in Man by Weiss' Method. The curve of the carotid pulse is shown above, the phonocordiogram in the middle, and the time markings of 0.01 sec. below. The curves are to be read from right to left. 1, 1, First sound; 2, second sound. (After O. Weiss, Phonokardiogramme, Jena, 1909.)

with a skin pencil and care should be taken to adjust the receiver to this point (a receiver placed inside the apex beat will often record the systolic retraction of the tissues near the apex giving the so-called "inverted cardiogram"). The jugular tracings are best taken with a Mackenzie cup about one and one-half

nches in diameter and slightly flattened on one edge. The cup is placed over the jugular bulb, just above and about one-half inch to the right of the right ster-

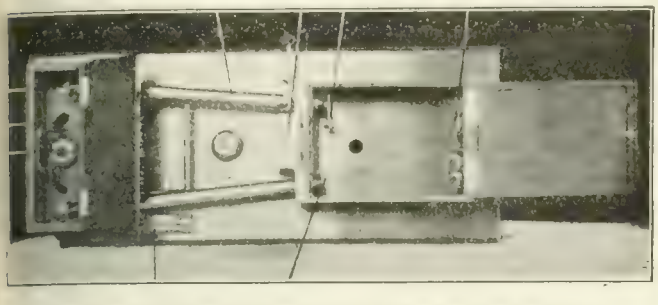


Fig. 1232.—Gerhart's Apparatus for Recording the Sounds and Movements of the Heart.

noclavicular junction, the flattened edge of the cup should be parallel to the upper border of the clavicle and should be held gently in position by the operator's hand, which is steadied by resting lightly on the chest wall; the cup is provided with a pin-hole vent, which may be covered by the operator's finger, who can thus adjust the internal air pressure without removing the cup. Any considerable pressure of the cup over the veins must be avoided The receiving cup may be shifted about to obtain the point of maximum venous pulsation; at times the best tracings are obtained at a point higher up on the neck.

In taking tracings of the movements of the liver a larger cup with a flattened edge should be employed; the abdomen should be relaxed and the cup brought in contact with the under surface of the liver.

Records of the left auricle have been taken by introducing into the esophagus a stomach tube with a single lateral opening covered with a delicate rubber membrane. The tube must be introduced to a point which brings the rubber membrane opposite the pulsating auricle. In taking such records a preliminary course of training is necessary to accustom the patient to the use of the tube.

The changes in air pressure produced in the various receiving devices are transmitted to the tambours connected with the writing levers by rubber tubing; each of these tubes should be provided with a small lateral valve closed automatically by a spring which can be released at any time to regulate the internal air pressure.

When all the levers are seen to be correctly adjusted and moving freely the time marker is started and finally the clock work moving the paper. At times when the respiratory movements distort the jugular tracing it will be found of advantage to have the patient hold his breath while the polygram is being taken. From time to time the paper should be stopped so that synchronous points on the various curves may be indicated for the sake of subsequent measurement. The smoked paper records are fixed by passing them through a bath of varnish.

The Interpretation and Significance of the Polygram.—The main facts of clinical importance which have been obtained from polygraph studies of the circulation have been derived from a comparison of the relations of auricular and ventricular activities. The value of records of the apex beat, carotid, brachial, or radial arteries depends on the fact that they represent more or less accurately the activities of the left ventricle, while the movements of the jugular veins or a pulsating liver give us a certain insight into the activities of the right auricle.

The diagram (Fig. 1234) indicates the internal pressures and time relations of the ventricle, auricle, and vessels of the normal subject.

In clinical work we usually make use of synchronous records of the radial and jugular tracings. The principal waves of the jugular tracing are, the wave of auricular systole (A); the wave synchronous with

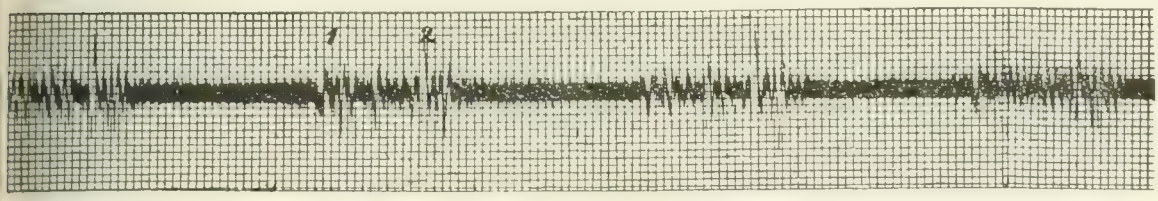


Fig. 1233.—Record of Heart Sounds taken with Einthoven's String Galvanometer. 1, First sound; 2, second sound. (*Johns Hopkins Hospital Bulletin.*)

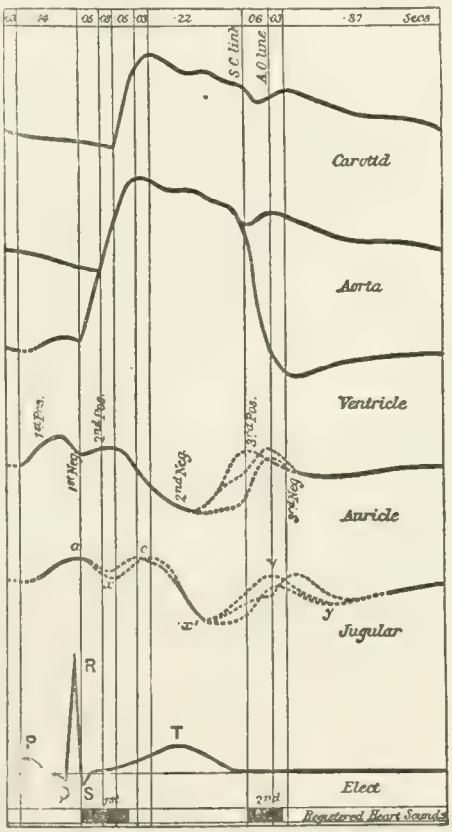


Fig. 1234.—Diagram of the Pressure Changes in the Cardiac Chambers and Their Time Relations to the Aortic, Carotid, Jugular and Electrocardiographic Curves and Heart Sounds. (After Lewis.)

and probably due to carotid pulsation (C); and the wave (V) due to rising auricular pressure during the ventricular systole. The depression (X) is mainly due to the relaxation of the auricle after its systole. The depression (Y) is due to the emptying of the auricle after the opening of the tricuspid valve. The closure of the semilunar valves is frequently marked by a notch in the ascending limb of the (V) wave. The opening of the tricuspid valve is indicated by the termination of the (V) wave (Fig. 1235).

The first step necessary in analyzing a jugular tracing is to locate the C wave. To accomplish this one measures accurately with dividers the distance of the foot point of any given radial wave from the line marking the beginning of the radial tracing; one then measures off a corresponding distance from the starting place of the jugular tracing; at a distance equivalent to 0.1 second preceding this point will be found the C wave (since the pulse wave requires 0.1 second to travel from the carotid to the radial at the wrist). In the normal tracing the A wave will be found preceding the C wave by 0.2 second. The V wave follows the C wave separated from it by the depression X. The depression Y follows the V wave.

Under various arrhythmic conditions of the heart there will be found variations in the relations of these waves of the jugular pulse; these variations afford us a means of determining the time relations of the auricular and ventricular activities and from these can be deduced certain abnormalities in the fundamental properties of the cardiac tissues. The polygram of the abnormal pulse will not be discussed here as it has been treated of at length in Volume I under the heading *Arrhythmia, cardiac.*

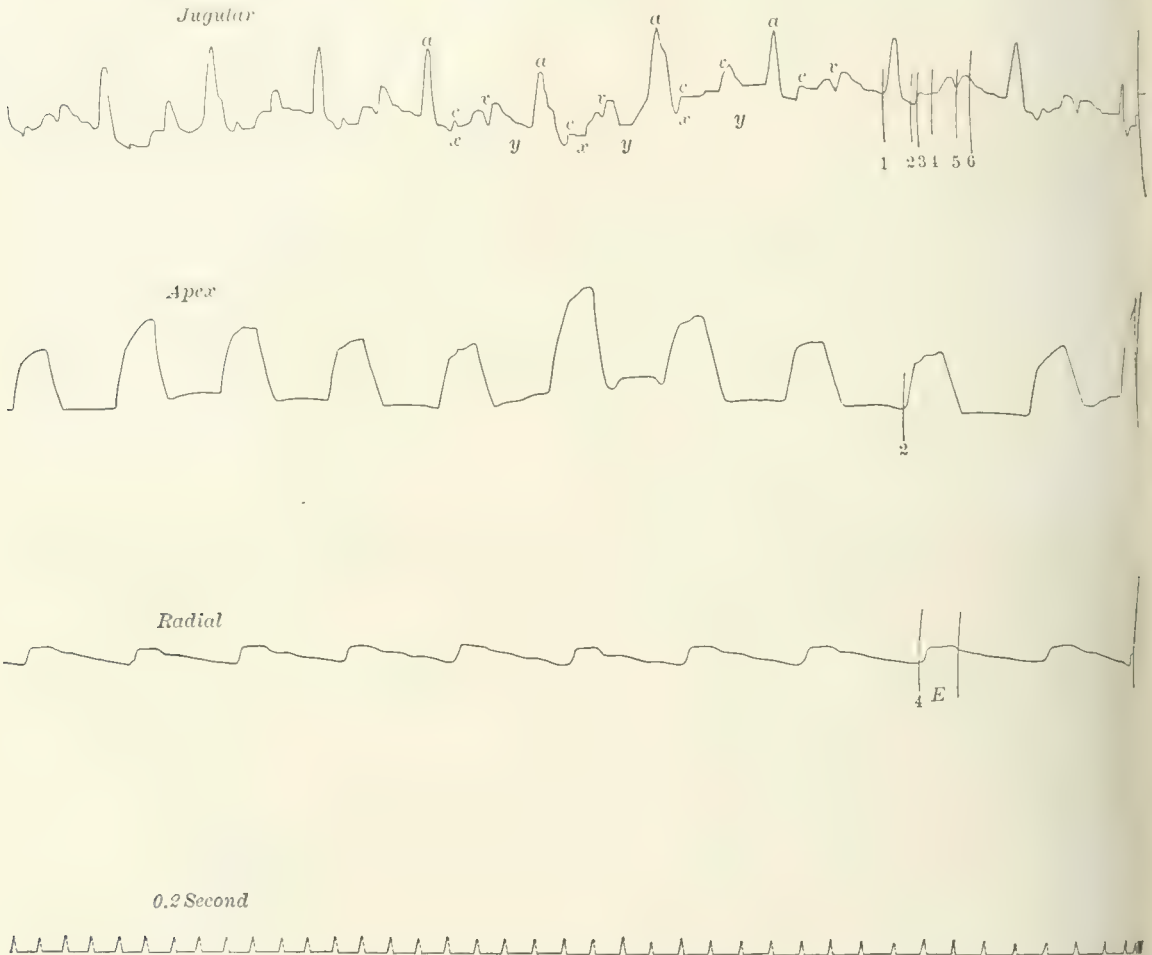


Fig. 1235.—Normal Polygram. 1, Beginning of auricular contraction; 2. beginning of apex contraction; 3, beginning of carotid wave 4, beginning of radial wave; 5, closure of semilunar valves; 6, opening of tricuspid valves; $E = 3$ to 5, ventricular systolic period.

Electrocardiography.—This is the art of recording graphically the differences in electrical potential of the heart muscle during its activity. That every contraction of a muscle is accompanied by certain definite changes in electrical potential has been known since 1856, when Kölliker and Müller detected the action current of the frog's heart by applying electrodes to its surface. When a wave of contraction passes over a muscle, that portion of the muscle which is actively contracting is electrically negative to all other parts of the muscle. It is the object of electrocardiography to detect those differences of electrical potential which occur during the contraction of the heart muscle and to record them graphically. This has been made possible clinically by the genius of Professor Einthoven of Leyden, to whom we are indebted for the construction of a wonderfully delicate galvanometer known as *Einthoven's String Galvanometer.* This instrument consists of a powerful electromagnet activated by a storage battery of five to six amperes furnishing about ten volts. Between

the poles of this electromagnet is stretched a delicate filament of platinum or of silvered quartz; the diameter of one of these threads is from two to four microns (about half the diameter of a red blood-corpuscle) and their resistance is about 5,000 ohms.

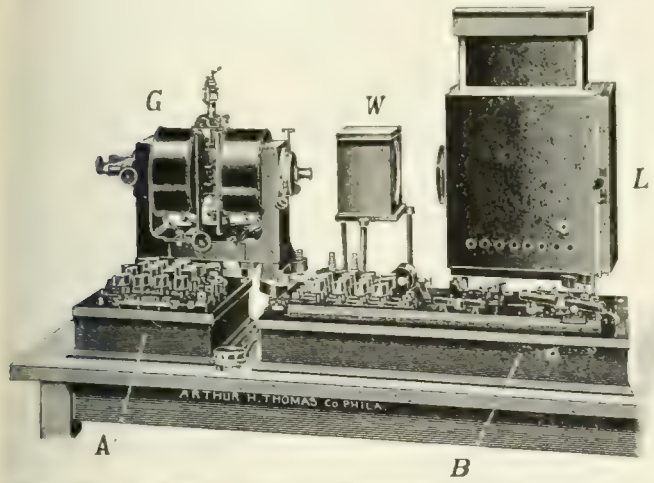


Fig. 1236.—Einthoven's String Galvanometer. *G*, Galvanometer; *L*, arc light; *A* and *B*, systems of plug rheostats. (Arthur H Thomas Company.)

When a current of electricity passes through this string, at right angles to the lines of force of the magnetic field of the electromagnet, the string is deflected to one side or the other according to the direction in which the current passes. An arc light connection with a rheostat is so arranged that the operator may send any desired fraction of this current through the string in either direction and thus determine the sensitiveness of the instrument at any particular moment. The tension of the string may be increased or diminished at will by means of a micrometer screw, thus readily varying its sensitiveness. The string is usually adjusted so that the passage of one millivolt of current causes a deflection of the shadow of one centimeter.

When a patient is placed in the galvanometer circuit by attaching suitable electrodes to the surface of the body, it is found that certain differences of potential are present which cause a deflection of the string (the so-called "skin current," probably due to the glandular activities of the body). In order that the delicate differences of potential of cardiac activity may not be obscured by this "skin current," it is neutralized by introducing into the circuit in the opposite direction, by means of a rheostat, a sufficient portion of the current from a single dry battery cell to exactly counterbalance the "skin current."

For the purpose of enclosing the patient in the circuit various forms of electrodes are employed, usually metal vessels containing solutions of common salt in which the extremities are immersed. A more satisfactory electrode devised by Dr. H. B. Williams is used in our work at the Presbyterian Hospital, New York. It consists of a large thin flexible sheet of German silver covered with light felt; this is moistened with hot salt solution and bound about the extremities with tapes.

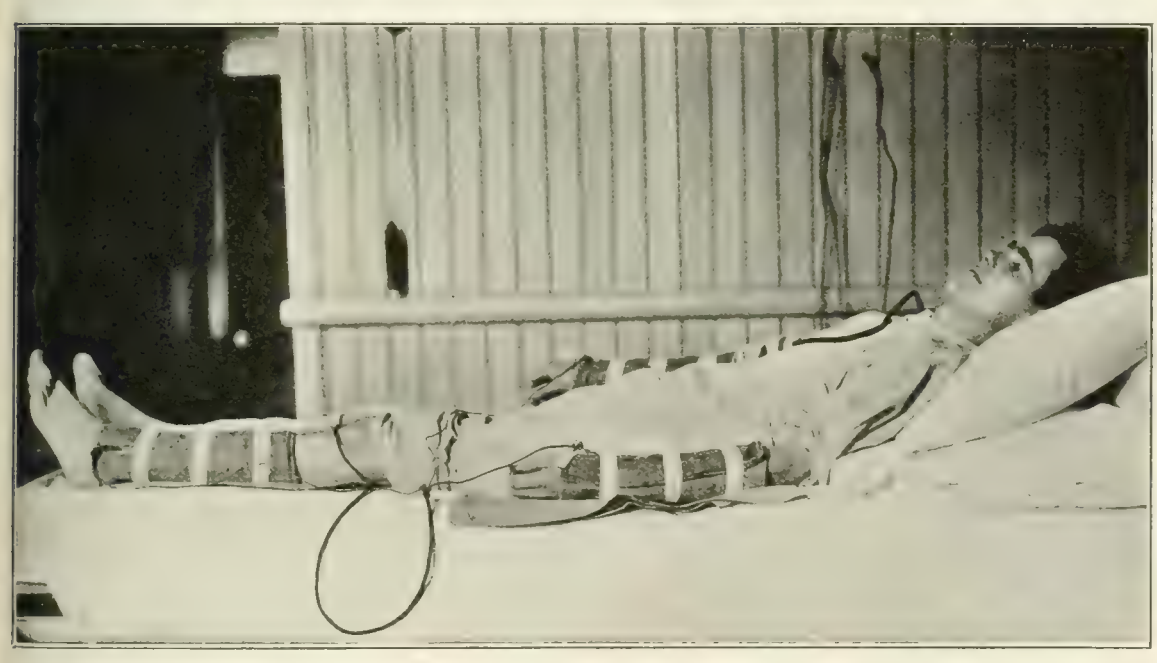


Fig. 1237.—Patient Prepared for Electrocardiography. Attachments made by means of Williams electrodes on arms and left leg.

passing through a system of condensing lenses and Zeiss objective and projection oculars, magnifies and focusses the shadow of the string on a photographic plate or film.

A Weston normal element furnishing one volt in

A Jacquet timer recording fifths of a second is placed in front of the camera so that the time intervals are recorded simultaneously with the movements of the string. The photographic apparatus which we have employed is made by Edelmann; it makes use

of a 200-foot kodak film moved by an electric motor, with convenient devices for numbering, exposing, cutting off, and removing the film according to the length desired. In the Presbyterian Hospital wires are run from the laboratory to the several wards so that records are easily taken of patients without removing them from their beds. Records thus taken at a distance are known as *telecardiograms*.

The patient under observation should be warm, relaxed, and perfectly quiet, since tenseness of the muscles, muscular movements, shivering, talking, coughing, etc., cause irregular movements of the

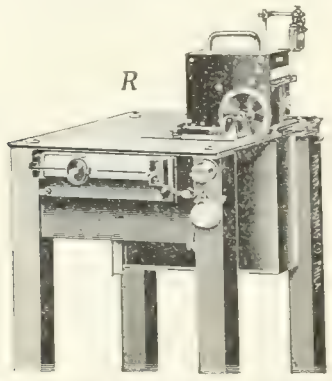


Fig. 1238.—Photographic Apparatus for Recording the Movements of the String of Einthoven's Galvanometer. (Arthur H. Thomas Company.)

string (these however are usually easily differentiated from the movements due to heart activity).

The character of the electrocardiographic curve varies with the parts of the body from which it is derived. In routine work it is customary to take three records from each patient designated as follows:

Lead I..... Current from right arm and left arm.
Lead II..... Current from right arm and left leg.
Lead III..... Current from left arm and left leg.

The steps necessary to be taken in making an electrocardiogram are as follows:

1. Attachment of three electrodes to the patient, (right arm, left arm, and left leg).
2. The estimation of the resistance in each of the three leads.
3. The standardization of the galvanometer.
4. The compensation of the "skin current."
5. The recording of the movements of the string of the galvonometer under the influence of the heart action.
6. The development and printing of the films.

The Interpretation and Significance of the Electrocardiogram.—When no current is passing through the

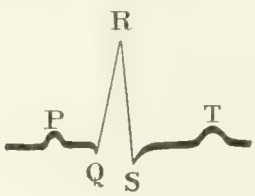


Fig. 1239.—Scheme of the Normal Electrocardiogram.

string of the galvanometer, the electrocardiogram presents a base line which shows the string at rest. When a current passes through the string it is deflected and these deflections are shown in the electrocardiogram as waves varying in height and length. The principal features and the lettering of the waves of the normal electrocardiogram as first suggested by Einthoven are shown in the diagram (Fig. 1239). The wave P corresponds to the systole of the auricles. The waves Q, R, S, T, correspond to the systole of the ventricles; of these waves R and T are most constant and are the best understood; Q and S may either one or both be absent in the electrocardiogram of the healthy subject. A satisfactory interpretation of all of the elements of the electrocardiogram is not yet possible, but the following summary indicates the significance of the main features as most generally accepted at the present time.

P = auricular systole.
P to R = the time occupied in the conduction of the impulse from the auricle to the ventricle = 0.12 to 0.17 second
Q = the first evidence of ventricular activity (probably portions of the ventricular muscle at some distance from the base).
R = activity of the basal portion of the ventricle.
S = activity of the apical portion of the ventricle.
T = final activity of the ventricle (probably the basal portion near the exit of the great arteries).
T to following P = diastolic period.

The electrocardiograms obtained from the normal individual by the three leads, as described in a preceding paragraph, present somewhat different features. The wave P is positive in all leads. The P–R interval varies slightly in the three leads. All the waves of lead II. are greater than those of leads I. and III. The wave R is positive in all leads. T is usually positive in all leads but is occasionally negative in lead III., even in normal individuals. There is a considerable range of variation in the electrocardiogram which lies within the limits of the normal. Among these physiological variations may be mentioned a shortening of the diastolic period in increased frequency of the heart; a variation in the amplitude of the R wave synchronous with respiration; increase in the size of the T wave with increased exertion; and changes in Q and S coincident with changes of the position of the heart in the thoracic cavity.

Hypertrophy of the heart is shown in the electrocardiogram by certain well-marked features. As was mentioned above, the normal heart shows R_I, R_{II}, and R_{III} all as positive waves. In hypertrophy of the left ventricle R_I is positive and relatively high and R_{III} is negative. In hypertrophy of the right ventricle R_I is small or negative, R_{III} is positive and relatively high.

Cardiac Irregularities.—This subject is treated at length in another volume, hence in the present paper only a brief outline will be given of a few of the features of the electrocardiogram which aid in their elucidation. The electrocardiogram records not only the time relations of the systoles of the auricles and the ventricles, but also the algebraic sum of the differences of potential of the heart muscle at any given moment, and certain other evidence from which we are able to determine the source of impulse formation and the direction in which the impulses travel. These features allow us to draw certain inferences in regard to the nervous control of the heart, the rapidity of impulse formation and the rhythmicity of their discharge, the conductivity of the cardiac structures and perhaps of their contractility. With such data we are frequently able to form a very definite opinion in regard to the prognostic importance of certain heart irregularities, to determine the site of certain lesions of the cardiac structures, and to determine the action and therapeutic results of various remedies.

The accompanying electrocardiograms reproduced from records of patients in our service in the Presbyterian Hospital and from private practice indicate a few of the features of the normal and abnormal electrogirocardam. (See Plate XXIII.)

Comparison of Polygraphic and Electrocardiographic Records.—In comparing the value of the polygram and the electrocardiogram as means of

EXPLANATION OF
PLATE XXIII.

EXPLANATION OF PLATE XXIII.

All figures are reduced one-third from the originals. In the originals the distance between the horizontal lines is two millimeters. In all the records the string is adjusted so that a millivolt of current deflects the shadow one centimeter. The lower line, made by a Jacquet chronograph, represents fifths of a second.

FIG. 1.—*Normal* E. K., lead I., right arm and left arm.

FIG. 2.—*Normal* E. K., lead II., right arm and left leg.

FIG. 3.—*Normal* E. K., lead III., left arm amd left leg.

NOTE.—P = auricular complex.
Q R S T = ventricular complex.
P, R, and T are positive waves.
Q and S are negative waves.
Relative heights of R in three leads.
Normal P–R interval.

FIG. 4.—*Sinus arrhythmia* probably due to vagus effect.

NOTE.—Variation in length of P–R (conduction) and of T–P (diastolic) intervals.

FIG. 5.—At X is shown a *ventricular extrasystole* which had its origin in the left side of the heart near the apex.

NOTE.—Abnormal form of P wave in the regular beats. Absence of P wave in the extrasystole. Compensary pause after extrasystole.

FIG. 6.—At X is shown an *auricular extrasystole* with origin high up in the auricle. The upper line is a pressure curve of the brachial pulse.

NOTE.—P occurs too early in the rhythm and is followed by a ventricular complex (R T) of normal form. Compensatory pause after extrasystole.

FIG. 7.—At X is shown a *nodal extrasystole* which has its origin low down in the auricle near the junctional tissues. The upper line is the radial pulse.

NOTE.—Reversed P wave followed by a normal ventricular complex. Compensatory pause after extrasystole.

FIG. 8.—At X is shown a *ventricular extrasystole* which has its origin in the right side of the heart near the base. The upper line is the radial pulse.

NOTE.—Absence of P before extrasystole which is followed by a compensatory pause. Large excursion of waves of extrasystole with relatively small effect on the radial pulse.

FIG. 9.—*Auricular fibrillation.* Auricular fibrillary waves shown at ff.

NOTE.—Complete irregularity, absence of P waves and normal ventricular complex (Q R S T).

FIG. 10.—*Tachycardia and alternation.* A series of ventricular extrasystoles. From a case of paroxysmal tachycardia. Rate, 222.

NOTE.—Every other wave varies in size. The auricle responds to the ventricle at every other beat (reversed P wave).

FIG. 11.—*Auricular fibrillation with coupled beats.* Digitalis effect.

NOTE.—Each regular ventricular beat (R) is followed by a ventricular extrasystole (X).

FIG. 12.—*Complete block.* Auricular rate, 120. Ventricular rate, 54.

FIG. 13.—*Paroxysmal tachycardia* composed of a series of ventricular extrasystoles.

NOTE.—Short paroxysm, rate 220. Reversed P every other beat. Sudden transition from slow to rapid rate. Abnormal ventricular complex of slow rate (seventy-five per minute) with abnormally long P–R interval. To the right is shown a single ventricular extrasystole with compensatory pause.

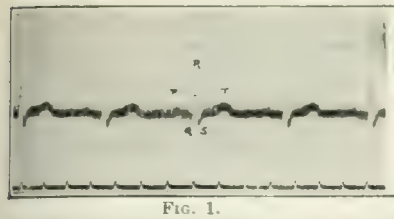
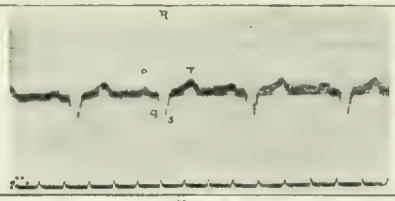


Fig. 1.



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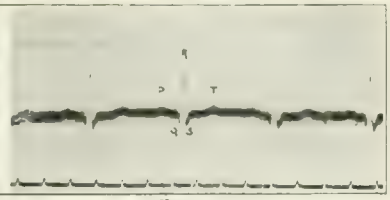

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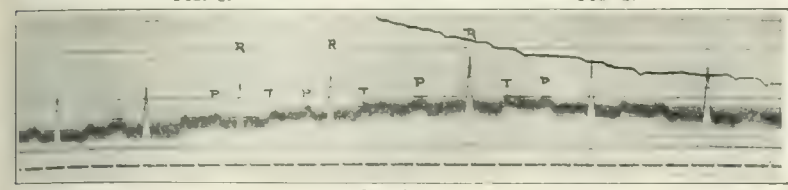
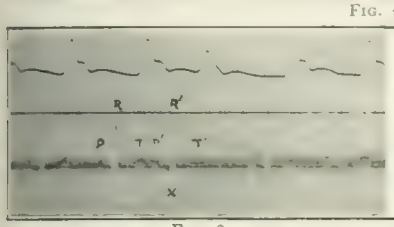


Fig. 4.

Fig. 5.



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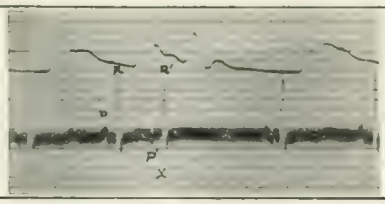

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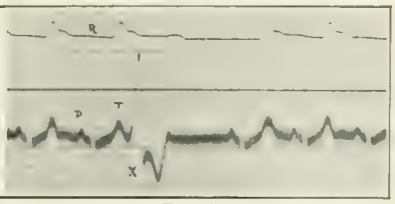

Fig. 8.

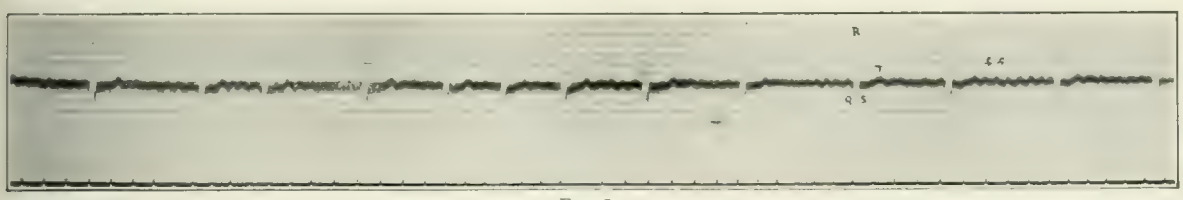

Fig. 9.

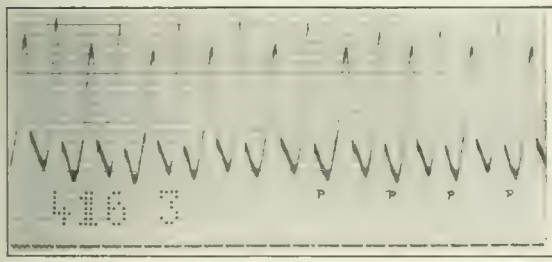

Fig. 10.

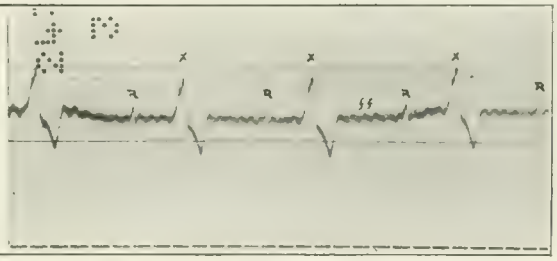

Fig. 11.

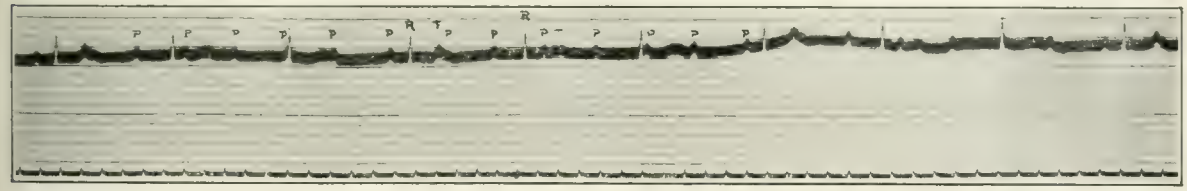

Fig. 12.

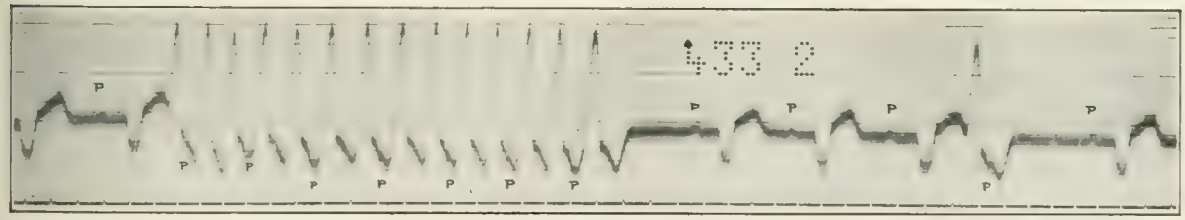

Fig. 13.

ELECTROCARDIOGRAMS.

interpreting the changes in the anatomical and functional condition of the heart we should observe first of all that these two methods record different sets of phenomena. The polygram, whether taken with the micrograph or with one of the several lever writing instruments, is a graphic time-pressure curve; the electrocardiogram is a graphic portrayal of the variations of electrical potential during muscular activity. By both of these methods we can study the functions of stimulus production, irritability, conductivity, and contractility, but each method has certain advantages and is successful in points where the other is inadequate. They do not portray the same phenomena and are therefore supplemental and corroborative rather than identical. For this reason we have adopted the scheme of taking what we call "combined records," *i.e.* we often record on the same film photographs of the electrocardiographic and "time-pressure" curves of the arterial and venous pulses. The conclusions drawn from both types of records are remarkably in accord, thus strengthening the evidence obtained.

Of the means at our disposal for taking polygraphic records, the micrograph is by far the most delicate. It registers not only the gross movements of the heart and blood-vessels but also such phenomena as thrills, heart sounds, etc. It is remarkably free from the errors of inertia which beset the lever writing instruments. It has the disadvantages of requiring a considerable degree of skill in its manipulation and of being moved from place to place with no small amount of trouble. It is essentially a laboratory instrument. As a rule the records obtained by this method cannot be read directly but must first be plotted, a feat which requires a considerable expenditure of time.

The ordinary lever writing polygraphs have the advantages of portability and of easy manipulation by those who are willing to devote a little time and patience to acquire the necessary skill: they are comparatively inexpensive in the first cost and up-keep. They have the disadvantage of producing tracings which may contain a considerable number of artifacts and errors of inertia.

The electrocardiograms are marvelous in their accuracy and wonderfully free from artifacts. Their value as precise records of cardiac phenomena is emphasized by the accuracy with which they repeat the minute characters of a given heart at intervals of months or even years. The string galvanometer of Einthoven is an expensive instrument which must be installed in a laboratory. It is not portable and can be used only for such patients as can be brought within the sphere of its electrical attachments. The time and skill necessary for its manipulation will confine its operation to the specialist.

The polygram records directly certain volume and pressure phenomena and conditions in the peripheral vessels and organs on which the electrocardiogram sheds light only by inference. The electrocardiogram on the other hand gives us direct information in regard to the position and size of the several parts of the heart and knowledge of the origin and course of impulses through the cardiac tissues, subjects which the polygram elucidates but little. With the aid of either of these methods we can study the relations of the activities of the auricles and the ventricles, the length of time required for the transmission of impulses, and many other features of the functional activity of the heart.

The efficiency of the heart is dependent on many factors, prominent among these is the sequence of the contractions of its several chambers and of their individual fibers. These graphic records reveal the presence of order or disorder in these events and help us to discern the particular kind of disorder which may be present. The records are of considerable value in forming a correct prognosis and as a means of watching the progress of cardiac changes in the individual case; they afford us direct indications for treatment and allow us to follow with precision the effect of the therapeutic measures employed.

The heart station at the Presbyterian Hospital, where these studies have been made, was erected by the liberality of Prof. Walter B. James and it has been under his direction and encouragement that this work has been carried out. His untiring enthusiasm is gratefully acknowledged as the exciting stimulus of the studies here presented.

T. Stuart Hart.

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Cardiolysis.—(From *καρδία*, the heart, and *λύσις*, a releasing). A term applied by L. Brauer, of Heidelberg (*Arch. f. klin. Chir.*, Berl., 1903, lxxi., 258), to a method of treating surgically adhesive mediastinopericarditis by resection of the regional costal cartilages and sternum. This operation was planned for cases in which external pericardial adhesions fix the heart, pericardium, and great vessels to neighboring organs, as the sternum, posterior mediastinum, diaphragm, and lungs. According to the position and firmness of these adhesions, the organs are forced to follow the movements of the heart, or they interfere with the action of the heart, such as emptying of the blood through the great vessels. The thorax in the entire cardiac area is retracted with each systole in wide extent.

Brauer's idea was that by breaking the elastic bony ring of ribs the heart might be relieved functionally. This does not mean a severe operation with disseverance of extensive adhesions, but only the substitution of a covering of soft parts for the natural bony covering of the heart. This was tried upon several patients, one of whom had adherent pericardium, broken compensation, ascites, and edema. Segments of the third, fourth, and fifth ribs seven to nine centimeters in length were resected. Recovery was uninterrupted. The pulse soon became stronger and more regular, the ascites and edema disappeared, and the patient could do heavy work without symptoms.

Brauer thinks that the suggestion of Delorme and Beck to dissever adhesions is not practical because too severe, and because adhesions would form again too rapidly. Morris Booth Miller.

Carduus Benedictus.—Also known as Blessed Thistle, Cursed, Holy, Bitter, or Spotted Thistle. It is the dried herb of *Cnicus benedictus* L. (Fam. *Compositæ*.) This is a large annual species of thistle, native of southern Europe. It is a largely used drug in Europe and is official in most European Pharmacopœias. It is quite largely imported into the United States, for medicinal purposes.

It is a stout and coarse plant, and is mostly chopped up into short pieces before being shipped. The stem is frequently reddish. The leaves vary from a foot in length and coarsely petioled below, to small and decurrent above, and are ovate, oblong, coarsely and sinnately pinnatifid and dentate, the teeth spiny-tipped, the spines being yellow, as are those terminating the involucral scales of the heads, which are

mostly more than an inch in length. The plant is of a yellowish-gray or whitish-green color, a peculiar agreeable odor and a very bitter, slightly salty taste. The akenes bear an outer pappus of ten short teeth, and an inner of ten short and ten long alternating ones.

The active principle appears to be the bitter glucoside *Cnicin*. The drug is a good simple bitter, and is also employed as a stimulating diuretic, a laxative, and an hepatic stimulant. The dose should represent thirty to sixty grains (2.0–4.0) of the drug. Cnicin is sometimes given in doses of five to eight grains (0.3–0.5). Overdoses may cause poisoning symptoms of emesis and catharsis.

H. H. Rusby.

Cargile Membrane.—A particularly thin gold-beater's skin made from the peritoneum of the ox, and adapted for surgical purposes by heat-cumol sterilization. It was devised as a substitute for Senn's omental grafting by Dr. Charles H. Cargile, of Bentonville, Arkansas, who, in March, 1900, sent a specimen to Dr. Robert T. Morris, of New York (*Medical Record*, 1902, i., p. 773), who first used it in a case of pyosalpinx "for the purpose of keeping separated peritoneal adhsion surfaces apart."

Morris experimented on twelve rabbits, and found that Cargile membrane resists absorption more than ten and less than thirty days, and protects areas of peritoneal surface whose endothelial covering has been impaired. He found it unnecessary to suture it in place as it adheres instantly to moist surfaces and is not readily dislodged afterward. It must not be handled with wet hands or instruments. Morris used it over growing epithelium, over exposed brain, making a good temporary dura mater, and around severed and sutured tendons. It has since fallen into disuse, and in its stead surgeons are now employing fascia lata, amniotic membrane, and egg membrane.

For further information consult: "An Experimental and Histological study of Cargile Membrane," by Craig and Ellis (*Annals of Surgery*, 1905, lxi., No. 6, p. 801) who conclude that it is not of value to prevent abdominal adhesions, but that until absorbed it acts as a foreign body, and therefore is an irritant.

Morris Booth Miller.

Caris.—A genus of ticks, family *Argasidæ*, with an almost circular body, a little larger in front than behind. Conspicuous transverse grooves behind the anus. Parasitic on bats. See *Arachnida*.

A. S. P.

Carlsbad (Karlsbad) is one of the most important thermal stations of Europe; indeed, its reputation is world-wide. It is charmingly situated in the northwestern corner of Bohemia, some seventy miles from Prague, at an altitude of about 1,160 feet, lying in the narrow valley of the Tepel River among the pine- and fir-clad hills traversed by paths in all directions. There are many beautiful walks and drives in the woods covering the slopes of the valley, and attractive excursions in the environs. "The valley in which it lies is shielded from the south and east winds by the mountains, but is exposed to the winds from the north and west, and the climate is consequently somewhat trying and subject to sudden changes in temperature" (Stedman). The native population is about 12,000, and upward of 30,000 people visit the springs annually.

These thermal waters are said to have been discovered in 1347, by the Emperor Charles IV., while hunting, but Carlsbad was known as a health resort a century earlier (Baedeker). "The springs issue from apertures in the rocky shell upon which most of the town is built, and are sixteen in number, all similar in their ingredients, which are principally sulphate of sodium, carbonate of sodium, and common salt. They are chiefly taken internally. They vary in temperature, the hottest having the least amount of carbonic acid gas. Some of the principal springs are the following with their temperatures (Fahrenheit scale):

"Sprudel, 162.5°—a steaming fountain leaping up at short intervals, and having a capacity of four hundred and fifty gallons per minute; Felsenquelle, 138°; Schlossbrunnen, 127°; Mühlbrunnen, 124.5°; Theresienbrunnen, 122°; Marktbrunnen, 118°. These waters are classed among the sulphated alkaline waters." The following is the composition of the Sprudel water, according to the analysis of Ragsky, as given by Stedman. Each liter (1.76 pint) contains:

	Grams.	Grains.
Sulphate of sodium	2.372	=35 58
Sulphate of calcium	.163	= 2.44
Chloride of sodium	1.030	=15.45
Carbonate of sodium	1.361	=20.41
Carbonate of calcium	.297	= 4.45
Carbonate of magnesium	.124	= 1.86
Carbonate of strontium	.0008	= .012
Protoxide of iron	.002	= .03
Protoxide of manganese	.0006	= .009
Fluoride of calcium	.003	= .045
Phosphate of calcium	.0002	= .003
Silica	.0072	= .108

Carbonic acid in one litre 210.59 c.c.

Although, as has been said, the waters are now used chiefly internally, there are seven bath houses with mineral, mud, vapor, hot air, and other baths, and with massage and Swedish movements. The Kaiserbad is said to be "one of the most magnificent bath houses of Europe." The conditions for which the internal use of Carlsbad water is beneficial are stated by Weber to be the following: In the first place, affections of the liver, including catarrhal jaundice, frequent attacks of biliary colic, early stages of alcoholic cirrhosis, enlargement of the liver in great eaters, etc. Secondly, habitual constipation, hemorrhoidal conditions in robust persons, some cases of chronic gastric and intestinal catarrh with or without diarrhœa, some cases of dyspepsia, uric-acid diathesis, chronic glycosuria in fat people, and corpulence, which is often combined with a weak-acting heart. Enlargement of the spleen is also said to be benefited by these waters, as are also periodic, frequently recurring headaches connected with abdominal disorders. Disturbances of the female pelvic organs, chronic congestion and enlargement of the uterus, chronic affections of the conjunctiva and deeper structures of the eye, and chronic aural catarrh are all likely to be benefited or cured by the Carlsbad waters.

During the summer the usual time for drinking the waters is from half-past five to half-past eight in the morning, an interval of about a quarter of an hour being allowed after each glass (℥ vi.), and the dose being from two to six glassfuls.

In beginning a course of treatment the spa physician carefully considers each case, and regulates the habits and diet of the patient. Probably the regularity in daily life and diet has very much to do with the improvement of the patient. The average daily programme of the ordinary Kurgäste is outlined by Weber as follows:

"Rise early to drink the water, and in the intervals promenade to the sound of the music; walk to some café, and take breakfast at about 9 A.M., consisting of coffee or tea, rolls, and perhaps boiled eggs or ham. At about one o'clock the chief meal of the day is taken; coffee and tea at about 4 P.M., and a light supper in the evening." Those who have been ordered a course of baths mostly take them in the forenoon. There are a fine Curhaus and a good theater; classical concerts are given regularly; there are covered walks; in brief, there is almost everything which will render the stay of the invalid agreeable and pleasant. There are also good educational facilities.

The season lasts from the middle of April to the end of September or October, although one can take the waters at any season of the year. Besides the amount of water drunk at Carlsbad, it is said that about 3,000,000 bottles of the water and 110,000 pounds of the salt are exported annually.

An after-cure is always recommended subsequent to a course at Carlsbad. Instead of returning home immediately, and at once resuming his or her usual mode of life, the patient should abstain from active work, adopt a simple diet, and live outdoors as much as possible for some weeks.

Carlsbad is reached by various routes in about thirty-one hours (from London): by Colonge, Würzburg, and Nürnberg or Bamberg; by Paris, Stuttgart, and Nürnberg; or by Cologne, Leipsic, and Dresden.

For the major part of the above account of Carlsbad, the writer is indebted to "Spas and Mineral Waters of, Europe" (by Hermann and F. Parkes Weber, London, 1896), to which the reader is referred for much valuable information upon this subject.

EDWARD. O. OTIS.

Carminatives.—A term (derived from Lat. *carminare*, to cleanse) applied to medicinal agents which relieve flatulence. They act chiefly by increasing or regulating gastric and intestinal peristalsis and so preventing spasm and causing the expulsion of flatus. They are frequently added to purgatives to prevent excessive and spasmodic peristalsis, which might otherwise result from the drastic action of these remedies, and so to avoid griping. When exhibited solely for the relief of flatulence they are frequently combined with an antacid such as sodium bicarbonate. The remedies usually classed as carminatives are the so-called stomachics, aromatics, spices, volatile oils, camphor, chloroform, hydrocyanic acid, and the ethers. These are given singly or combined, as in Dalby's carminative (mistura carminativa N. F.), Parrish's camphor mixture (mistura camphoræ aromatica N. F.), soda mint (mistura sodæ et menthæ N. F.), Godfrey's cordial (mistura sassafras et opii N. F.), pulvis aromatica U. S. P., pulvis cretæ aromaticus N. F., pulvis rhei et magnesiæ aromaticus N. F., spiritus ammoniæ aromaticus N. F., elixir chloroformi compositum N. F., etc. T. L. S.

Carnine, $C_7H_8N_4O_3+H_2O$, is one of the substances found in commercial meat extract. It has also been isolated from the flesh of fish and from human urine. Carnine is related to hypoxanthine, being transformed into the latter by oxidation.

FRANK P. UNDERHILL.

Carnitine, $C_7H_{15}NO_3$, is a strong base, probably a trimethylamine derivative, present in commercial meat extracts. F. P. U.

Caroba.—A name applied to the leaflets of several species of *Jacaranda* (fam. *Bignoniaceæ*), small trees of Brazil, especially of *J. procera* (Willd.) Spreng. and *J. caroba* (Vell.) D. C. They contain resinous and slightly aromatic constituents, and the crystalline, apparently inactive body *carobin*, but nothing to which any special medicinal properties can be assigned. The drug bears a high reputation and is largely used in Brazil as a remedy for syphilis and syphilitic disorders. This belief, which applies to so many plants of little or no activity, doubtless results from the indefinite ideas which prevail regarding syphilis, all sorts of venereal and many other diseases being included under this name. The drug is generally given in the form of the fluid extract, in doses of ♏ xv. to lx. (1.0–4.0).

HENRY H. RUSBY.

Carota.—*Carrot.* The root of *Daucus carota* L. (fam. *Umbelliferæ*). This plant is a native of Europe, but freely naturalized in the United States (wild carrot). The cultivated form is the common table carrot, grown everywhere. The fruits of wild carrot have been used as aromatic diuretics; the cultivated roots are made into pulp as poultices; but neither have any claim to medical notice. The coloring matter of carrot root is called *carotin*. The very small amount of volatile oil consists of pinene and probably cineol.

H. H. RUSBY.

Carotid Gland.—(Synonyms: Ganglion intercaroticum; Glandula carotica; Glomeruli arteriosi intercarotici; Nodulus intercaroticus.)

This little-known organ lies in the bifurcation of the common carotid artery, generally near the posterior side of the internal carotid just as it comes off the main trunk. In size it averages five millimeters in length, two to five millimeters in thickness, and three millimeters in breadth (Gomez), varying considerably. Because of its great vascularity the color is pink. For some time it was thought to be an epithelial organ developed similarly to the thyroid and thymus from the branchial clefts, but further study showed it to be of entirely different origin and nature. Its embryonal origin is later than the thyroid and thymus, and it is in no way related to them, for it arises directly from the primary vascular *anlage*, and therefore is not an epithelial, but a perithelial, structure. The first step in its formation consists

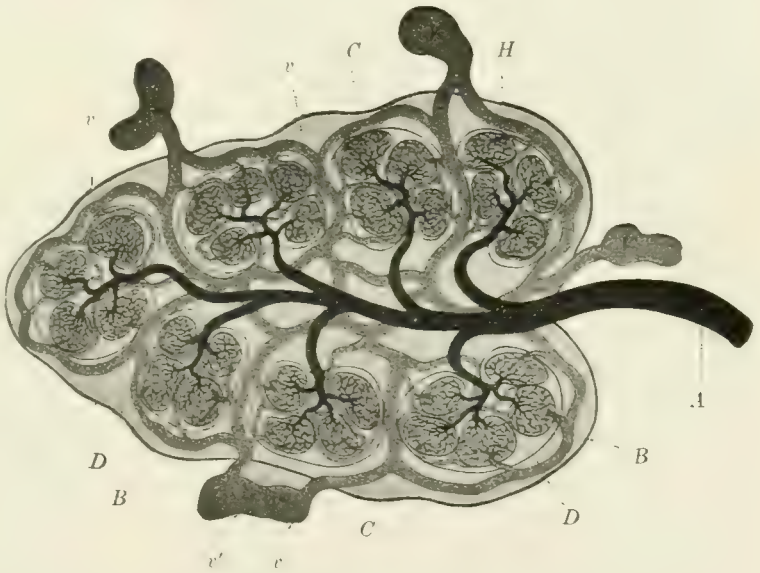

FIG. 1240.—Scheme of Circulation and Structure of the Carotid Gland, showing its Glomerule-like Character. (After Schaper.) *A*, Principal artery with *V*, corresponding vein; *B*, balls of cells; *C*, capillary networks; *D*, secondary nodules; *H*, hilus; *v*, *v'*, smaller veins.

of a cellular thickening of the external posterior portion of the periphery of the embryonal carotid. At this time the cells, of epithelioid type, are not distinguishable from the cells of the vessel wall itself, and the gland anlage is recognized merely as a thickening of the cell mass at this point. This entire nodule is surrounded by the adventitia, and over it run nerve bundles from the vagus and cervical sympathetic. Very early in its development capillary vessels derived from the common carotid at its bifurcation enter the cell mass, and soon form glomerule-like collections, which with the rapidly increasing cell growth soon distinguish the gland from the vessel. It increases in size until the third decade.

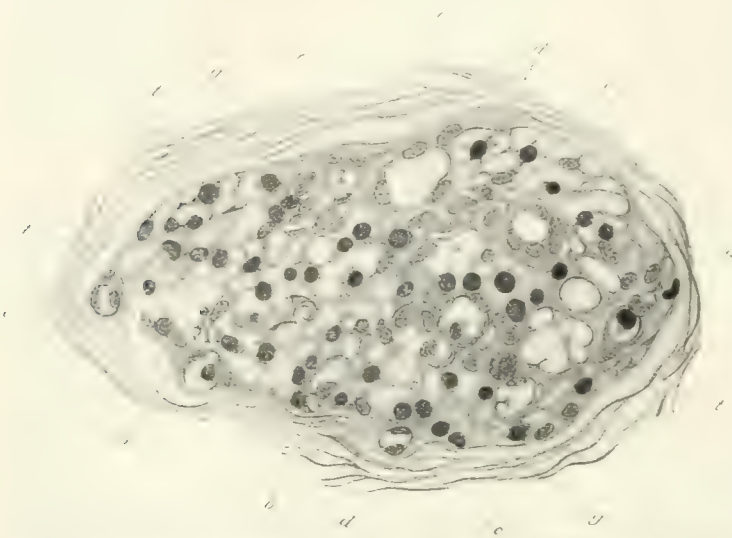

FIG. 1241.—Section of a Lobule of the Carotid Gland. × 520. From a man fifty years of age. (After Schaper.) *a*, Smallest arteriole; *b*, connective-tissue reticulum; *c*, capillaries; *d*, nuclei of stroma; *g*, protoplasmic network; *t*, nuclei of gland cells.

In the adult the carotid gland shows a lobular structure. From the connective-tissue capsule, bands pass into the organ, carrying many vessels and nerves, and dividing it into lobules, which vary in number from three to twelve. In turn the lobules are composed of small "cell balls," which really form the unit of its structure. These consist of a glomerule-like tuft of capillaries that unite to form a vein. Surrounding the capillaries are the cells of the organ, arranged in cords or trabeculæ, although this arrangement is not at all evident in ordinary preparations. The number of cells about individual vessels varies greatly; sometimes there is quite a wall of epithelioid cells, with finely granular cytoplasm, oval nucleus, and a nucleolus, but often there is but a single layer of cells about a vessel, or the vessels may be separated merely by a loose reticular interstitial connective tissue. In this reticular tissue are frequently single cells of the same type. Often the parenchyma cells show a considerable degree of vacuolization, particularly in the old. According to Gomez there are two types of parenchyma cells, differing in the amount of chromatin and the size of the nucleus. It is said that with age the typical structure becomes less and less evident, accompanied by more or less disappearance of these special cells, and increase of the fibrous tissue. The structure of the carotid gland is quite similar to that of the coccygeal gland.

The function of the carotid gland is altogether unknown. It seems to have been the subject of but little investigation except by histopathologists. It is undoubtedly closely related to the sympathetic nervous system, as shown by the number of ganglion cells and nerve fibers from the cervical ganglia, and by the presence of the same cells with affinity for chromic acid and its salts, the so-called "chromophile" cells that are found also in the sympathetic glands, adrenals, and coccygeal gland. In the few recorded cases of tumors of this gland there have been no symptoms that could be considered indicative of any function, and the unilateral resection of the gland in these cases has been followed by no symptoms whatever. Extracts from the gland are said to raise the blood pressure greatly.

PATHOLOGY.—Except for tumor growths there seem to be few records of pathological alterations in this organ, probably because it escapes observation through its location and its minute size. Gomez found that it shows a sclerosis in direct proportion to the amount of sclerosis in the carotid artery, whether senile or syphilitic; in acute infectious diseases it rarely shows parenchymatous degeneration; no other lesions were observed in some fifty autopsies.

Keen and Funke were able to collect in the literature from 1891 to 1906 reports of 27 cases of tumors of the carotid gland which had been operated upon, besides two observed at autopsy. Of these 27 cases, 17 were in patients from 13 to 35 years of age, 7 between 36 and 50, and only 2 after 50 years of age; there were 14 in males and 15 in females. These tumors are characterized by their location in the crotch of the carotid, with which they are so intimately connected that the vessel usually must be ligated and cut across in the operation for removal of the tumor.

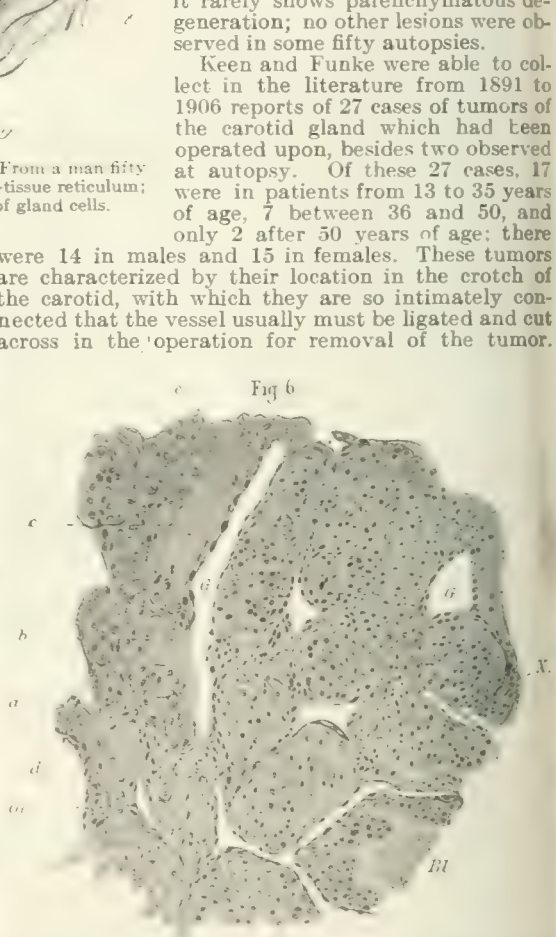

FIG. 1242.—Perithelial Tumor of the Carotid Gland. (After Paltauf.) *G*, Vessels; Bl, blood extravasation; *a*, hyaline degeneration of cells; *b*, hyaline degeneration; *c*, hyaline masses.

Some of the tumors are quite benign in character, but frequently they are very malignant; in five cases metastasis in the regional lymph glands was observed, and in several of the patients operated upon a speedy recurrence followed. They usually produce few sub-

jective symptoms, although occasionally headache, hoarseness, and narrowing of the pupil have been observed. They are commonly localized by a well-defined capsule, divided by fibrous septa, and the color is extremely variable. The tumor is rather firmly fixed, because of its relation to the carotids, and for the same reason it frequently transmits pulsation which has led to a diagnosis of aneurysm. In the other cases tuberculous cervical glands and thyroid tumor have been suspected. The diagnosis has usually been made only at operation, when the location of the tumor in the bifurcation of the carotid is quite characteristic. Clinically this relation to the artery, the slow growth in the early history, the elastic consistence, and the scanty subjective symptoms are suggestive features.

The malignant tumors of the carotid gland testify to its origin in the perithelium, for they form quite typical perithelomas. The tumor is generally highly vascular, and about the capillaries are layers of epithelioid cells, with a strongly staining oval nucleus, and considerable finely granular cytoplasm. The thickness of these walls seems limited by distance from blood-supply, and the perithelial cells tend to form cords with central spaces lined solely by the tumor cells. The lobular structure of the gland is retained, as well as its richness in vessels and nerves.

H. Gideon Wells.

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Carpenter, William Benjamin.—Born in Bristol, England, in 1813. He received the degree of Doctor of Medicine from the University of Edinburgh in 1839. After practising for a short time in his native city, and delivering lectures on medical jurisprudence, he was made Professor of Physiology in the Medical School of the London Hospital. In 1839 he published his first book of any importance ("Principles of General and Comparative Physiology, etc."); and not long afterward he published his "Treatise on Human Physiology"—one of the most clearly written and most practical text-books on physiology in the English language. Carpenter is also the author of many treatises of a popular character. He was burned to death on November 10, 1885, while taking a hot-air bath. A. H. B.

Carroll, James.—Born in England in 1854, but came to this country in early life. In 1874 he enlisted as a private in the U. S. Army, and was soon promoted to be a sergeant. He was for fifteen years a hospital steward, studying medicine in his leisure moments. In 1891 he was graduated from the Medical Department of the University of Maryland, and afterward took postgraduate courses in pathology and bacteriology at the Johns Hopkins Hospital. He was then appointed contract surgeon, but in 1902, in recognition of his services on the Yellow Fever Commission, the age limit was waived and he was allowed to appear for examination for admission to the Medical Corps, and was appointed first lieutenant and assistant surgeon. A few years later Congress passed a bill authorizing his promotion to the rank of major and surgeon in the regular army. Owing to his cardiac disability, Dr. Carroll was not fit for active service, and was appointed curator of the Army Medical Museum. He died September 16, 1907.

Carroll was a member, with Lazear and Agramonte, of the U. S. Army Commission in Havana created, with Major Walter Reed as its head, to study the cause and mode of spread of yellow fever. While serving on this Commission he voluntarily submitted to the sting of a mosquito which had previously bitten three persons suffering from yellow fever. Four days later he was stricken with a severe attack of the disease from which he finally recovered—more fortunate than his colleague Lazear—but which left him with a crippled heart that caused his death. T. L. S.

Carthamus.—*Safflower, African or dyer's saffron, False, American* or *Thistle saffron,* consists of the florets of *Carthamus tinctorius* L. (fam. *Compositæ*). Although called American saffron, this plant is of Oriental nativity. It is widely cultivated for ornament and also, to some extent, for the product here described. It produces handsome large flower heads, of an orange-yellow color, at the ends of the branches. From these the florets are plucked out, dried, and constitute the drug. They were formerly largely used for dyeing purposes and are still so used to a considerable extent in India. They constitute a red or deep orange-red mass, of a rather slight characteristic odor and an aromatic and bitterish taste. The individual florets are about two centimeters ($\frac{3}{4}$ in.) long, though often broken, tubular, and very deeply divided into five linear and nearly equal lobes. The stamens have long exserted coherent anthers and a slender style which is considerably longer than the stamens. The ovary should not be present. The principal coloring matter of safflower is deep yellow and constitutes one-fourth or more of the weight of the drug. It is known as *safflor-yellow* ($C_{24}H_{30}O_{15}$) and is soluble in water. There is also a fraction of one per cent. of the red coloring matter *carthamic acid* or *carthamin* ($C_{14}H_{16}O_7$), which is not soluble in water but gives a beautiful purple color in alcohol. The latter coloring matter exists in commerce as a reddish-brown, somewhat metallic powder. It is used in rouge-making. The properties and uses of safflower differ but little from those of saffron, and its principal use is in fact the substitution of the latter.

H. H. Rusby.

Cartilage.—Under this name is classified one of the important members of the group of connective tissues; it is characterized not so much by the structure and arrangement of its cells, as by the peculiar nature of its basement substance. Cartilage occurs in three tolerably distinct forms, the differences of which depend largely upon peculiarities in the structure of the basement substance. These forms are called *hyaline cartilage, fibrocartilage,* and *fibroelastic cartilage.*

Hyaline Cartilage.—The most abundant and typical of these is hyaline cartilage. This, in the adult, is found covering the articular surfaces of bone, forming parts of the ribs and of the walls of the trachea and bronchi, and in less considerable masses in other parts of the body. Hyaline cartilage is translucent and of a bluish-white color, is firm in consistency, and elastic. Like other members of the connective-tissue group, it consists of cells and an intercellular or basement substance, commonly spoken of as the matrix. The basement substance is for the most part quite homogeneous in the fresh condition, but it is occasionally very finely granular. By suitable treatment with chemical agents, it may be seen to contain, and almost to consist of, exceedingly minute and delicate fibrils, which under normal conditions are merged into a homogeneous mass; the same results may also be obtained by prolonged maceration and pressure. The basement substance is said by some observers to be penetrated by minute

branching canals which communicate with one another and with the spaces in which the cells lie. Mucin and gelatin, and a rather indefinite substance called chondrin, have been obtained from the basement substance, but our knowledge of the chemical nature of these substances, and particularly of their existence in the cartilage in the natural condition before being exposed to chemical manipulation, is still too indefinite to enable us to speak very positively of its chemical constitution. The fibrous character of the matrix and the presence therein of mucin and gelatin suggest that this cartilage is closely related to fibrous connective tissue.

The cells of hyaline cartilage differ considerably in shape and arrangement in different cartilages and in different parts of the same cartilage, depending, apparently to a considerable degree, upon the conditions of pressure to which they are subject, as well as upon the intimate constitution of the basement substance and the influences under which its development transpires. The cells, except near free surfaces or where cartilage and fibrous tissue join, are in general spheroidal, ovoidal, ellipsoidal, or somewhat flattened at the sides, and lie unevenly distributed in the basement substance. The cell body is finely granular, or in some animals contains delicate fibrils, and may enclose droplets of fat and pigment particles, or may also contain glycogen. The nuclei —of which there may be one or more—are usually spheroidal, sharply outlined, and contain more or less well-marked networks of coarser and finer fibrils and nuclei, in which, during life, in some animals, slow oscillatory movements may be seen. The cartilage cells may lie singly in the basement substance, but they are more frequently arranged in groups of two or four, or more, and the cells forming these groups are apt to be flattened on the sides which abut on one another. Under normal conditions the cartilage cells completely fill the spaces in the basement substance in which they lie. But on exposure to the air, to water, to electric shocks of moderate intensity, to a variety of chemical agents, and under

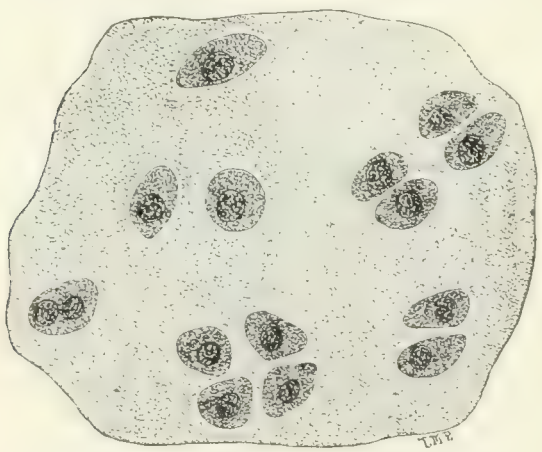

Fig. 1243.—Hyaline Cartilage from the Head of the Femur of a Frog. (× 700 and reduced.)

certain pathological conditions, they separate from the walls of the spaces and shrink into irregular-shaped, coarsely granular masses, in which the nucleus may be partially or entirely concealed. This shrinkage may be only partial, some portion or points remaining adherent to the sides of the cavities, so that the shrunken cells may appear irregularly stellate or have festooned edges. In this shrunken condition we usually see the cells of cartilages which have been preserved in alcoholic fluids. In some parts of the articular, and also in the costal cartilages, the cells lie in large groups, or in longer or shorter rows. At the free surfaces of cartilage, or where it comes in contact with the perichondrium, the cartilage cells are usually flattened, and just beneath the perichondrium may merge imperceptibly into the ordinary flattened cells of the connective tissue. The basement substance immediately about the cartilage cells may be seen, under favorable conditions, to be more transparent than the rest, the more transparent zone being sometimes very thin and sometimes of considerable thickness. This portion of the basement substance is called the capsule, and is believed to be that part which was last formed around the cartilage cell. Somewhat similar appearances may be seen not only around single cells, but around all groups which have apparently been derived from some single cell originally occupying their position in the basement substance. These capsules stain more deeply with basophil stains than the rest of the matrix; and the dark capsule with its group of cells therein form globular masses which have been termed a "chondrin ball" (Mörner).

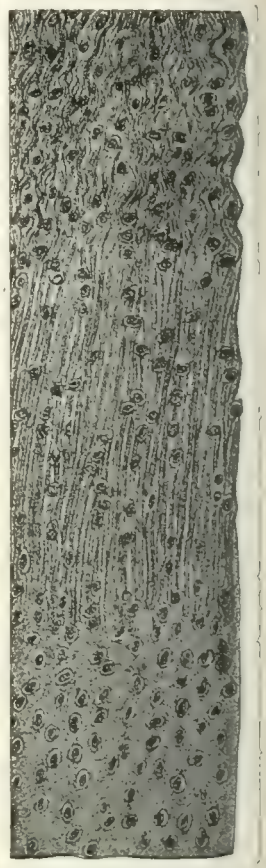

Fig. 1244.—White Fibrocartilage from the Ligamentum Teres at the Point where it is Inserted into the Head of the Femur. × 650 diameters. (After Böhm and Davidoff.) *a*, Fibrous connective tissue; *b*, fibrocartilage; *c*, point of insertion of the ligamentum teres; *d*, hyaline cartilage.

The basement substance of hyaline cartilage may, under a variety of conditions, become infiltrated with salts of lime, and thus assume to the naked eye a white, opaque appearance, and under the microscope appear crowded with larger and smaller distinct granules. Under pathological conditions the basement substance may become fibrillar as well as calcified. Cartilage is surrounded, except over the articular surfaces, by a vascular layer of fibrillar connective tissue called the *perichondrium*. The perichondrium contains a varying amount of elastic fibers. The fibrillated fibers of the perichondrium pass on into the hyaline basement substance of the cartilage, into which they become gradually merged. Although vessels from the perichondrium sometimes penetrate for a short distance into the cartilage tissue, the latter is, in general, non-vascular.

Development of Hyaline Cartilage.—At a very early period hyaline cartilage, which originates in the mesenchyme, consists of a congeries of rounded cells closely packed together, with a small amount of intercellular substance around each cell. The intercellular substance gradually increases in amount, and the cells divide; new capsules, *i.e.* new portions of intercellular substance, are formed around the new cells, while the old capsules are expanded and appear to coalesce with those of adjacent cell groups to form

the homogeneous basement substance. In this way the cells become gradually separated from one another, but may still retain a grouping which indicates their primitive relations.

Schleicher has shown that in the division of cartilage cells, while the changes in the nucleus are in general those common to the indirect mode of cell division (see *Cell*), the separation of the body occurs, not by a gradually deepening constriction, as in cells which are surrounded by a fluid or yielding material, but by the formation of a partition out of the intracellular filaments. This partition finally becomes continuous with the capsule around the new-formed cells, and thickens with their separation from one another. The exact way in which the capsules and intercellular substance originate, whether by a separation of a portion of the periphery of the cells, or

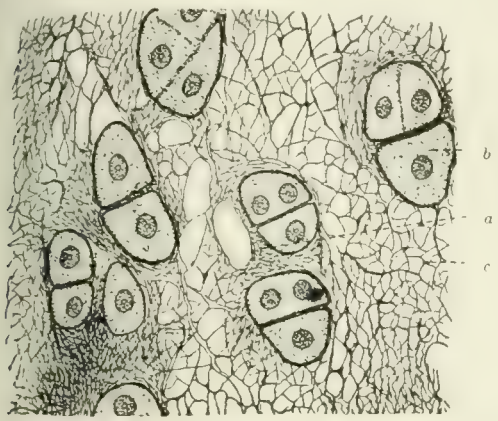

Fig. 1245.—Elastic Cartilage from the Human Ear. × 760 diameters. (After Böhm and Davidoff.) At *a*, in the immediate vicinity of the cartilage capsules, a network of elastic fibres with fine meshes; *b*, cartilage cell; *c*, elastic fibres.

whether it is simply formed under their influence, or entirely apart from them, is not certain. In the further development, a distinction arises as to whether the cells continue to proliferate rapidly, or divide but slowly. In the latter case each capsule becomes invested by another, and so on until there is an entire series of concentric capsules, which ultimately become a homogeneous matrix. In rapid proliferation the daughter cells quickly form their proper capsules and the ultimate result is the same.

Fibrocartilage.—This variety of cartilage is found in the interarticular cartilages of some of the joints, such as the knee and jaw, between the vertebræ at the symphysis pubis, around the tendons of certain muscles, and at points where tendons are inserted into hyaline cartilage, as at the junction of the ligamentum teres with the head of the femur. The cells are similar to those of hyaline cartilage, but the basement substance is fibrillated, the fibrillæ being arranged in dense bundles or interlacing in all directions. The cells are frequently arranged in rows between the bundles of intercellular fibers (see Fig. 1244), and are less uniformly distributed than are the cells of hyaline cartilage. This form of cartilage frequently merges, in structure, on the one hand into fibrillar connective tissue, and on the other into hyaline cartilage. As a rule the fibrous tissue greatly predominates.

Fibroelastic Cartilage.—This form of cartilage (yellow elastic or spongy cartilage) is not abundant in the body, being found in small masses in the external ear, Eustachian tube, epiglottis, and in some parts of the larynx. It is tough, opaque, and yellowish in appearance. The cells, which are irregularly distributed through the basement substance, are similar in appearance to those of hyaline cartilage. Around each cell is a narrow, strongly refractile, homogeneous zone of basement substance—the capsule. Outside of the capsule the basement substance is more or less densely filled with coarser and finer anastomosing and interlacing elastic fibers (Fig. 1245). In addition to the elastic fibers the basement substance contains numerous large and small granules, consisting of a material similar in chemical and optical properties to that composing the elastic fibers—the so-called elastic granules. These elastic granules are unevenly distributed through the basement substance. Fibroelastic cartilage is developed from a hyaline form of cartilage by the formation, in the basement substance, of the characteristic elastic fibers and granules. T. Mitchell Prudden.

Cartilage, Bones, and Teeth, Chemistry of.—Cartilage.—The organic basis of cartilage was formerly known as chondrigen and the gelatin-like substance obtained from it on boiling was known as chondrin; but it is now recognized that the so-called chondrigen is a mixture, containing the following as its chief constituents.

1. Collagen, resembling closely that of connective tissue.

2. An insoluble albuminoid substance, resembling elastin but richer in sulphur.

3. A mucin-like substance, known as chondromucoid and capable of decomposition into a protein and chondroitic acid.

4. Chrondroitic acid or chrondroitin-sulphuric acid, present in combination in chondromucoid and also uncombined. Schmiedeberg ascribes to chondroitic acid the formula $C_{18}H_{27}NSO_{17}$.

Of the cartilage cells little is known, but they contain traces of glycogen and fat.

The inorganic constituents of cartilage are characterized by the abundance of sodium which in adult mammals is principally combined with sulphuric acid. In mammalian embryos and in lower vertebrates the sulphuric acid is largely replaced by chlorine. In old age a gradual disposition of lime salts occurs leading to partial ossification. The composition of cartilage is summarized by Hoppe-Seyler as follows:

In 1,000 parts.	Costal cartilage.	Articular cartilage.
Water	676.6	735.9
Solids	323.3	264.1
Organic	301.3	248.7
Inorganic	22.0	15.4

Salts in one hundred parts of ash:

Potassium sulphate	26.66
Sodium sulphate	44.81
Sodium chloride	6.11
Sodium phosphate	8.42
Calcium phosphate	7.88
Magnesium phosphate	4.55

Bone.—The bones of vertebrates consist essentially of an organic basis of ossein and the so-called bone earths made up of inorganic salts. Elastin, fat, proteins, and nuclein are also present; the latter two principally from the bone corpuscles. Ossein, a scleroprotein, is identical with or very similar to the collagen of connective tissue. In the bone earths calcium predominates in the bases, but small quantities of magnesium are also present and traces of potassium and sodium. These bases are for the most part in combination with phosphoric acid, but some carbonic acid is found, and traces of chlorine and fluorine. The sulphuric acid mentioned by some writers is probably derived from

some of the organic constituents and does not properly belong to the bone earths. There is some difference of opinion as to how the bases and acids are combined, but according to Gabriel the simplest expression for the composition of the ash is $Ca_3(PO_4)_2 + Ca_5HP_3O_{13} + Aq$, in which two to three per cent. of the lime is replaced by magnesia, potash, and soda and four to six per cent. of the phosphoric acid by carbon dioxide, chlorine, and fluorine. As age advances the mineral constituents of the bone diminish somewhat while the organic components are slightly increased (Sappey and Nélaton). This fact is explained by the partial replacement of true bone tissue by enlarged blood-vessels and bone-marrow. Hoppe-Seyler gives the following composition for undried bone without separation of marrow or blood: Water, 50 per cent.; fat, 15.75 per cent.; ossein, 12.40 per cent.; bone earths, 21.85 per cent. The composition of the bone earths is given as follows by Zalefsky in parts per thousand:

	Man.	Ox.
Calcium phosphate, $Ca_3P_2O_8$	838.9	860.9
Magnesium phosphate, $Mg_3P_2O_8$	10.4	10.2
Calcium combined with CO_2, Fl, and Cl	76.5	73.6
CO_2	57.3	62.0
Chlorine	1.8	2.0
Fluorine	2.3	3.0

Bone marrow is composed chiefly of fat (96 per cent.), containing the fatty acids of ordinary adipose tissue in the proportion of palmitic acid 22, stearic acid 10, and oleic acid 63 per cent. of the total fatty acids. Among the extractives of marrow are lactic acid, hypoxanthin, and cholesterin. Protein is present in small quantities, especially in the red marrow of the spongy bones. It is principally in the form of globulin and nucleo-albumin, with traces of albumin. Red marrow differs from ordinary yellow marrow in containing less fat but large numbers of red corpuscles. It also contains several peculiar iron compounds of whose composition little is known but which are believed to have something to do with the formation of red corpuscles.

Teeth.—These consist of crusta petrosa, dentine, and enamel. The crusta petrosa is a true bony structure and resembles ordinary bone in composition. Dentine is very similar in composition, but contains less water. Enamel is an epithelial structure containing scarcely any water but rich in lime salts. Its organic constituents are very small in quantity and differ from the ossein of bone and dentine in not yielding any gelatin on boiling. The following composition is given for the teeth by Hoppe-Seyler from analyses by Aeby:

Constituents.	Dentine.	Enamel.
$Ca_{10}CO_3(PO_4)_6$	72.06	96.00
$MgHPO_4$	.75	1.05
Organic substances	27.70	3.60

Wesley Mills.
William S. Morrow.

Carum.—Caraway. The dried ripe fruit of *Carum carvi* L. (fam. *Umbelliferæ*). The spelling of the specific name "carvi" is a relic of the use of but one character for both our *u* and *v*. The sound is, therefore, that of *u*, from which comes the pronunciation *caraway*. This is a biennial herb, with a long, brown, tapering, edible root, a slender, erect, branching, hollow stem, bi- or tri-pinnate leaves, with narrow linear segments, and small, compound umbels of white flowers. It is a native of Northern and Central Europe and Asia, and is cultivated and naturalized in nearly all temperate countries. The dried fruits, usually separated into their mericarps, are from three to five millimeters long ($\frac{1}{5}$ in.), slender, slightly curved, tapering at each end, and marked with five fine yellow ribs, alternating with dark brown intervening spaces. There is one large oil tube between every two adjoining external ribs, and two on the ventral face, six in all. The characteristic odor and taste are familiar to nearly every one. The active constituent is carvone, which constitutes fifty to sixty per cent. of its four to seven per cent. of volatile oil, and which can advantageously be substituted for the latter. Most of the remainder is limonene. There is also some fixed oil, resin, gum, sugar, and tannin. The stimulant and carminative properties are those of the family. The odor and taste are characteristic, and make of it and its oil a favorite flavoring. It is mostly used as an ingredient of bread and cakes. The medicinal dose is gr. viij. to xxx. (0.5–2.0). It enters into the Compound Tincture of Cardamom, the only official preparation.

Fig. 1246—Caraway Fruit. Enlarged about four times. (Baillon.)

The so-called "Black caraway," also largely used by German bakers, is not at all related, being the seed of *Nigella*. This contains, besides a volatile oil of very agreeable flavor, and much fat, about 0.5 per cent. of the alkaloid *damascenine*. The seed closely resembles the deadly larkspur seed.

Oil of Caraway (Oleum Cari).—A volatile oil existing in caraway to the extent of from four to seven per cent. It has the characteristic odor, taste, and properties of caraway. Its specific gravity is 0.905 to 0.915 at 25° C. (77° F.). It is soluble in an equal volume of alcohol. It consists of carvol and dextrogyrate limonene (*carvene*). The dose is ♏ i. to x. (0.06–0.6), but it is preferable to use carvol. It enters into the *Spiritus Juniperi Compositus*, its only official preparation.

Carvol ($C_{10}H_{10}O$).—A ketone which constitutes the essential constituent of oil of caraway, and which also occurs in oil of dill and oil of spearmint. It is a colorless, or pale yellow, transparent liquid, having a specific gravity of 0.960 and boiling at 224° C. One cubic centimeter diluted with the same amount of alcohol should at most assume only a slightly reddish or violet tint on the addition of a drop of a very dilute solution of ferric chloride. It has the odor, taste, and properties of oil of caraway, and is, in addition, quite uniform. It is official in the German Pharmacopœia. The dose, if the preparation is pure, is ♏ i.–v. (0.06–0.3). Henry H. Rusby.

Carus, Karl Gustav.—Born at Leipzig, Germany, in 1789, and educated in the same city. After taking systematic courses in chemistry and in medicine, he was appointed a Privatdozent in the University of Leipzig in 1811. Up to that time no lectures had been given at Leipzig on comparative anatomy—that branch of medical science in which Carus was particularly interested, and in which he proposed to give instruction—and it was therefore a source of great satisfaction to him when he discovered, as he soon did, that his reputation as a teacher was steadily increasing. In 1814 he was made Professor of Comparative Anatomy at the new medical school at Dresden, and in 1827 he received the appointment of Royal Physician. He died on July 28, 1869.

Of his numerous published writings the following deserve to receive special mention: "Grundzüge der

vergleichenden Anatomie und Physiologie," Dresden, 1828; "Atlas der Kranioskopie," Leipzig, second edition, 1864; and "Vergleichende Psychologie," Vienna, 1866. A. H. B.

Carvacrol.—*Oxycymol. Cymophenol.* ($C_6H_3.CH_3.[CH_2.CH_2.CH_3]6H$). This is one of the active constituents of oils of thyme and summer savory, and occurs also in some other plants. It is a thickish volatile liquid, with a specific gravity of about 0.981. It has a characteristic odor. Like thymol, with which it is associated, it is strongly antiseptic. It is very closely related to carvol, having the same composition.

HENRY H. RUSBY.

Caryocinesis.—See *Cell* and *Mitosis*.

Caryolysis.—KARYOLYSIS. This term denotes the change (called also *chromatolysis*) observed in the nucleus of a necrotic cell whereby its chromatin either entirely disappears or loses its staining power. Such change may be due to a solution of the nucleus, to chemical changes in the chromatin, or to its complete destruction. It is the most important microscopical evidence of necrosis, and is to be regarded as the essential feature of this process. The term is used synonymously with chromatolysis, but is gradually replacing the latter word.

ALDRED SCOTT WARTHIN.

Caryophyllus.—CLOVES. The dried flower buds of *Eugenia aromatica* (L.) O. Kuntze (Fam. *Myrtaceæ*).

Cloves are produced by a beautiful, fragrant, evergreen tree, with a fine pyramidal crown thirty or forty feet high, native of the Molucca and Philippine Islands, but now known only in the cultivated state, at least so far as the production of cloves is concerned. The chief production is in the East Indies and eastern Africa. The flowers, when expanded, are of a brilliant crimson, but the buds are gathered as cloves, before the petals expand. The quality of the product depends largely upon the buds being picked in exactly the right stage of development, and the best cloves are carefully picked by hand, after which they are quickly dried in the sun. Three flowers are borne together on a peduncle about a third of an inch in length, many of which become mixed with the cloves, and are regarded as an adulterant. They contain much less oil than the cloves, and are often distilled, under the name of *clove stalks*, for their oil, which is of good quality. Their presence in ground cloves is indicated by an abundance of stone cells, which are wanting in cloves. If both stone cells and starch are found, they indicate the presence of the clove-fruits, called *anthophylli*, or *mother of cloves*. "Exhausted cloves," those from which the oil has been removed, have also been largely used to adulterate the ground article. Cloves are a little over half an inch long, dark brown, consisting of a subcylindrical, solid, and glandular calyx tube, terminated by four teeth, and surmounted by a globular head, formed by four petals, which cover numerous curved stamens and one style. Cloves emit oil when scratched, and have a strong aromatic odor, and a pungent, spicy taste.

OLEUM CARYOPHYLLI.—Cloves contain a large percentage of the official oil, which sometimes forms as much as one-fifth of the weight. There are also present tannin, gum, resin, etc.; *caryophyllin*, $C_{20}H_{32}O_2$, which is isomeric with camphor; and *eugenin*, none of which is of any therapeutic value. The properties of the clove are contained in the volatile oil. It is obtained by distillation, and is official in all pharmacopœias. When first procured, the oil is clear and colorless and very fluid; with age and exposure it becomes yellow in color, and ultimately reddish brown. It also becomes thicker. Its specific gravity should be 1.040 to 1.060 at 25° C. (77° F.) It is soluble in equal volumes of alcohol, ether, and acetic acid. It is slightly acid in reaction. Oil of cloves is made up of *eugenol*, of which the U. S. P. requires the presence of not less than eighty per cent., by volume, *eugenic acid*, $C_{10}H_{12}O_2$, chemically resembling phenol and guaiacol, and a terpene, $C_{15}H_{24}$, which is deposited when the oil is kept for a length of time.

Eugenol is formed by a process of oxidation from oil of cloves, and may also be procured from other essential oils, as those of cinnamon, pimento, and sassafras. It is an aromatic, colorless, or brownish, oily liquid, insoluble in water, soluble in alcohol, and forms compounds of a definite character with caustic alkalies. It possesses antiseptic properties, and has been recommended as a febrifuge, but is inferior to salicylic acid, quinine, etc. Eugenol, the action of which is somewhat analogous to guaiacol, was brought into prominence by Dr. Koch, who suggested its administration during the tuberculin treatment. The dose is ♏ xlv. during the day, dissolved in spirit and diluted with water. Applied locally it has a mild anesthetic action.

Two derivatives of eugenol—benzoyl-eugenol and cinnamyl-eugenol—have been introduced and are advocated for the treatment of tuberculous disease. Both of these preparations occur in neutral, acicular crystals, free from color and odor; taste, faintly bitter; slightly soluble in water and freely soluble in alcohol.

The *therapeutic action* of cloves is due to the volatile oil which they contain, and is that common to all aromatic oils. Externally it is antiseptic, stimulant, and, when freely used, is a counterirritant. It also is slightly anesthetic. It is employed locally only as a remedy for rheumatic pains, sciatica, and neuralgias. Its most common use is as an antiseptic and anesthetic application to carious teeth.

When taken internally it produces a stimulating and antiseptic effect upon the mucous membrane of the stomach and bowels. It also acts as a carminative and antispasmodic, checking fermentation and promoting digestion.

After absorption it produces a general stimulation and is excreted unchanged by the kidneys, liver, and bronchi. Upon these tissues it exercises its antiseptic properties, and it is thought that this is specially directed to the pulmonary tissues. It is this local action upon the lungs which, with its carminative and stimulating effects, has encouraged its employment in tuberculosis.

The oil is usually selected for administration in from one- to five-drop doses. The average dose of powdered cloves is four grains. That of the oil is three minims. H. H. RUSBY.

Caryorrhexis.—KARYORRHEXIS. The term applied by Klebs to that form of nuclear fragmentation (called also *chromatokinesis*) in which the chromatin becomes broken up into small particles. It is distinguished from caryolysis in that in the latter process there is a complete disappearance of the chromatin, while in the former the nucleus is broken into particles which may be clumped on the nuclear membrane (hyperchromatosis of the nuclear membrane). Caryorrhexis is one of the earliest signs of necrosis, and is in the majority of cases a forerunner of caryolysis. The latter may occur, however, without a preceding caryorrhexis, the nucleus losing its staining power without undergoing fragmentation. According to Schmaus and Albrecht, the disintegration of the nucleus in caryorrhexis is not due to a rupture of the nuclear membrane, but is caused by definite and fairly typical movements on the part of the chromatin elements in response to certain influences acting from without the nucleus. The transposition of the chromatin elements is usually preceded by a condition of

hyperchromatosis leading ultimately to a separation of the chromatin into single particles which gradually lose their staining power. The phenomena of caryorrhexis may be observed in all forms of beginning necrosis due to any cause, but can be studied to best advantage in the necrosing areas of malignant tumors, particularly in carcinoma.

ALDRED SCOTT WARTHIN.

Casanthrol.—A thick and gelatinous emulsion of neutral reaction, composed of casein ointment and ten per cent. of lithanthracic extract. The latter consists of those constituents of coal tar which are soluble in benzol and ether. Casanthrol is soluble in water and when applied to the skin dries like a coat of varnish. However, being pervious to water, it does not prevent, but rather, if anything, tends to increase, the perspiration. It is precipitated by mineral acids, acid salts, and calcium salts; no oil separates from it on warming, and it does not become rancid. Classing it among his water-soluble varnishes Unna considers it a valuable application in chronic eczema and other chronic conditions of the skin. It is said to have been used in eczema and prurigo with no unpleasant secondary effects. It is the strongest coal-tar preparation which can be employed in inflammatory conditions of the skin; and if desired it may be used as a vehicle for other drugs. W. A. BASTEDO.

Cascara Amarga.—*Honduras Bark.* The bark of *Picræna vellozii* Engl. or of a related species, or, according to some authors, of an undetermined species of *Tariri*, syn. *Picramnia* (fam. *Simarubaceæ*). This bark comes from Central America, and is a very highly esteemed vegetable bitter by those who are accustomed to it. There is, with its strongly bitter taste, a peculiar sweet and aromatic flavor not resembled by any other drug. It contains a small amount, about one-half per cent., of volatile oil and about three per cent. of the alkaloid *picramnine*. The latter has the peculiar sweet and bitter taste of the bark and is probably its principal active constituent. It, as well as its salts, is amorphous. It is a simple or slightly aromatic bitter of unusually pleasant flavor. Its use as an alterative in syphilis is common, but we have no evidence of any special properties in this direction. The dose is gr. v.–xv. (0.3–1.0).

HENRY H. RUSBY.

Cascara Sagrada.—*Rhamnus Purshiana; Chittem Bark; Sacred Bark.* "The thick bark of the trunk and branches of *Rhamnus Purshiana* D. C. (fam. *Rhamnaceæ*)." (U. S. P.) The genus Rhamnus and the nature of its species and their constituents are discussed under *Frangula*. The species here considered is a small tree growing very abundantly in our extreme Northwestern States and northward. It was introduced into the materia medica in 1878 and encountered a remarkable degree of prejudice and opposition, being practically boycotted by many of the most influential physicians. It, however, steadily increased in favor and is at present probably the most largely used in professional practice of any American drug. During its early history, the bark of a related species, *R. californica* Esch., growing abundantly in central and southern California, was frequently substituted for it, but persistent exposure resulted in completely stopping the fraudulent practice, so that adulteration and substitution are now almost entirely unknown. The bark is taken off in quills, but these are afterward broken up to save space in transportation. These quilled pieces are of variable thickness, up to nearly one-quarter of an inch. The outer surface is rarely fissured, but is more or less warty, the warts being low and broad. The surface is originally of a peculiar red-purple or purple-brown, but becomes more or less covered with gray lichens. These may grow so as to form a uniform gray covering or a series of gray patches of variable size. Pieces taken from the base or junction with the root, are frequently thrown into transverse wrinkles or semi-folds. The inner surface when fresh is light-yellow, but exposure turns it gradually darker until after two or three years it may be nearly black. The fracture is sharp and of a pale yellow. There is a slight odor and a peculiar bitter and somewhat aromatic taste. Preparations of the drug are apt to have a very disagreeable taste and numerous formulæ have been devised for avoiding this unpleasant feature.

COMPOSITION.—The composition of cascara sagrada is very similar to that of buckthorn in its general nature, though certain differences are manifest. The frangulin-like body is not identical, and the percentage of *emodin* is much smaller. There is a much larger amount of resin and this is divisible into three distinct bodies. It is not clear to which of these differences the more regular and less griping characters are due. Throughout the recent active discussion of the presence of emodin, or emodin-like substances (*anthraquinones*) as active constituents of some of our most important cathartics, there has been shown a disposition to overrate the effect of such presence as determining similarity of action. It by no means follows that other constituents are to be ignored in the laxative effects, merely because the anthraquinones are thus active; besides which, we have to reckon with minor differences in the anthraquinones themselves. The distinctly bitter properties of cascara sagrada make it more effective in stimulating appetite and digestion. Like buckthorn, it is much more useful when given in small doses, for some time, to overcome habitual constipation, than when used as a cathartic. It has been at various times claimed as a useful agent in the treatment of rheumatism, syphilis, and similar diseases, and it is so by virtue of its depurative and eliminative properties, but not in any way as a specific. The actual physiological action of cascara sagrada has never yet been worked out, but it is evident that it in some way profoundly modifies the secretory and excretory functions. There is an official extract, of which the average dose is four grains. The fluid extract also is official. The dose as a cathartic, taken at night, is fl. ʒ ss. to i. (2.0–4.0). Those few who find their rest thus disturbed may take it in the morning, or may take a smaller dose. As an alterative or tonic laxative, the dose is ♏ xv. to xxx. (1.0–2.0), preferably before meals. Licorice, alkalies, and carminative oils tend to disguise the bad taste.

None of the extracted so-called active constituents of the drug are worthy to be compared to its galenical preparations. HENRY H. RUSBY.

Cascarilla.—The dried bark of *Croton eleuteria* Bennett (fam. *Euphorbiaceæ*) (N. F., B. P.). This species of Croton is a large, widely branched shrub of the Bahama Islands where it is rapidly approaching extermination, through destructive collection.

Cascarilla was imported into Europe about the middle of the seventeenth century, when it was considered a variety of cinchona. It has undoubtedly formerly been the produce of several species of *Croton*, but at present comes exclusively from the one above named. It is in quills or curved pieces, about one-twelfth of an inch (2 mm.) thick, having a somewhat fissured, easily detached, brown, corky layer, more or less gray from a covering of lichens, and the inner surface smooth. It breaks with a short fracture, having a resinous and radially striate appearance. When burned, it emits a strong, aromatic odor. Its taste is warm and very bitter.

The active principles of this bark are *cascarillin*, a white crystalline, bitter substance, scarcely soluble in water, to which it owes its tonic properties, and an *essential oil*, which latter it contains to the extent of something more than one per cent. It also contains much *resin* and a little tannin.

The composition just given indicates the use and value of cascarilla. It is a bright, rather pleasant, aromatic, bitter tonic, with no special qualities other than its taste, to distinguish it in medicinal value from other spicy bitters. It is used occasionally in pastils, and is said to be put into tobacco on account of its fragrance when burning. Alcohol extracts its virtues to the best advantage. Dose, as a tonic, gr. xv.–xxx. (1.0–2.0). There is no official preparation. The chief use of this bark is for incense in churches.

The section *Eleuteria*, of the enormous genus *Croton*, contains thirty or more plants, a number of which have barks possessing properties similar to those of cascarilla.

H. H. Rusby.

Caseation.—See *Necrosis*.

Casein.—This substance is the chief protein constituent of milk, occurring nowhere else in nature. The quantity present in milk varies with the species of animal from which the milk has been obtained. Casein belongs to the group of compound proteins, the phosphoproteins, and hence is chiefly characterized by containing an appreciable quantity of phosphorus in organic combination. Casein being insoluble in dilute acids is precipitated when the lactose ferments (when milk turns sour). It is also peculiar in its behavior toward the rennet enzyme, the latter causing the formation of a heavy curd. Unlike most native proteins casein does not coagulate on boiling. Instead its solutions, like milk, when boiled are covered with a thin pellicle; at the same time casein loses some of its sulphur. It has thus far been impossible to determine definitely whether the caseins from different kinds of milk are identical. However, the evidence available seems to indicate that each casein is peculiar to its own type of milk.

Frank P. Underhill.

Casein Ointment.—A thick, white emulsion, miscible with water and proposed by Unna as a vehicle for the application of drugs to the skin. Its formula is: Casein, 14; potassium and sodium hydroxides (1 to 4), 0.43; glycerin, 7; vaseline, 21; salicylic acid or borax, 1; water, 56. As it dries it leaves a thin coating upon the skin.

W. A. Bastedo.

Caseoiodine.—A substance of the nature of thyreoiodine stated to have been used with good results in myxedema. The edema subsided, the hair and skin became soft, the intelligence clearer, and the phlegmatic condition gave place to one of average activity. It is prepared from per-iodo-casein, and is a white powder containing 8.7 per cent. of iodine. The dose is gr. $\frac{1}{6}$ (0.01) once or twice a day, increased rapidly up to gr. i. (0.06) a day. In overdose it is capable of producing flushing, rapid weak heart, and prostration.

W. A. Bastedo.

Cashew Nuts.—*Anacardium*. The ripened ovary, with contents, of *Anacardium occidentale* L. (fam. *Anacardiaceæ*), a large, widely sprawling shrub, or small tree, of tropical America, largely cultivated in all tropical countries for its fruit. The edible portion of this fruit consists of the fleshy enlarged pedicel, and is of the form and size of a medium pear, green or yellow with a red cheek. It is juicy to an extraordinary degree, and is consumed chiefly for its thirst-quenching properties. Unless thoroughly ripe, it is exceedingly astringent. When ripe, the juice is slightly sweetish and slightly acid. This fruit is also manufactured into a wine which is credited in Brazil with special properties as an hepatic stimulant. The ripened ovary, many times smaller than the fleshy portion, is partly hidden in the summit of the latter. It is kidney-shaped, about three centimeters (1.2 in.) long, brownish-ash colored, and smooth externally. It contains a large, bland, oily, curved, edible embryo. The pericarp, which is two or three millimeters ($\frac{1}{8}$ in.), thick, is of cavernous structure, and contains, when dry, a thick or solid, black, extractiform, resinous substance, of exceedingly irritant properties when applied to the skin. A bassorin-like gum exudes from the stem; an edible milky sap, which also is an indelible dye, flows from the trunk.

The resinous extract consists of *anacardic acid*, and a yellow or brown oily liquid, *cardol*. This is an intense and dangerous irritant, causing often severe inflammation of the skin and blisters, and even the fumes, when it is burned, are said to have the same properties. It was formerly used as an irritant, and is still so used to some extent in the West Indies. It has no medicinal value here, and is only to be known as a poison. The roasted and salted kernel is a delicious table delicacy.

The East Indian *anacardium* is a smaller but similar product, from *Semecarpus anacardium* Linn. *fil.*, in the same family. A milder cardol, "*Cardol pruriens*," is obtained from its fruit, and has been used also as an irritant, and as a basis of indelible ink. It is now entirely out of use on account of the danger attending it. Poison ivy, *Rhus toxicodendron* L., and poison sumach, *Rhus venenatum*, are in the same family, and, as well as some other species of *Rhus*, have a similar inflaming action upon the skin (see *Poisonous Plants*).

H. H. Rusby.

Cassebohm, Johann Friedrich.—One of the most skilful anatomists of the eighteenth century. He was born about 1705 in the vicinity of Halle, Prussian Saxony, and received his medical education partly at the University of the latter city and partly at Frankfort-on-the-Oder. He probably also spent a certain length of time at Paris, for Haller speaks of him as having been a pupil of the Danish anatomist Winslow, who resided in that city during the years 1669–1760. In 1738 he was chosen Professor of Anatomy at the University of Halle, and three years later he was asked to fill the same chair at Berlin. He died on February 7, 1743, leaving behind him, although he was comparatively a young man at the time of his death, a well-established reputation as an anatomist.

His published writings are few in number, but of exceptional merit. The titles of these are as follows: "Dissertatio de aure interna," Frankfort-on-the-Oder, 1730; "Programma de differentia fetus et adulti anatomica," Halle, 1730; "Tractatus quatuor anatomici de aure humana, tribus figurarum tabulis illustrati," Halle, 1734; and "Tractatus quintus anatomicus de aure humana, etc.," Halle, 1735. According to the statement of Dezeimeris, Haller owned at one time the manuscript of a very remarkable work, entitled "On the Art of the Anatomist." This work, of which Cassebohm was known to be the author, constituted in reality a complete treatise on anatomy.

A. H. B.

Casserio, Giulio.—Born in Placenza, Italy, in 1545. His parents being poor, Casserio was obliged to go out to service. Fortunately for him, as it afterward turned out, the person by whom he was employed was Fabrizio d'Aquapendente, the distinguished anatomist. The latter soon noticed that Casserio possessed a decided aptitude for scientific studies, and he accordingly aided the young man in every possible

manner to pursue the career of physician. After his pupil had secured the degree of Doctor of Surgery and Philosophy, Fabrizio still further honored him by calling upon him from time to time to lecture in his place. Finally, in 1604, when Fabrizio's poor health compelled him to resign his chair, the Senate of Venice gave the position to Casserio, who performed its duties, during a period of several years, with great credit to himself.

Casserio holds a high rank in the history of anatomy. He made numerous discoveries, among the more important of which may be mentined the following: he was the first to describe correctly the two apophyses of the malleus and the muscles attached to the ossicles of hearing; he ascertained the fact that the canal of the cochlea has no outlet in its upper portion; he described correctly the cartilages and muscles of the larynx; and he was the first to give an exact description of the operation of tracheotomy and to furnish pictorial illustrations of the instruments required for its performance. (The structure which is often termed the "Casserian ganglion" was not discovered by Casserio, but by a German Surgeon named Gasser.) Of the books which he published the following two deserve specially to be named: "De vocis auditusque organo historia anatomica," Ferrare, 1600; "Tabulæ anatomicæ LXXVIII.," Venice, 1627. A. H. B.

Cassia.—See *Cinnamon.*

Cassia Fistula.—Purging Cassia. The ripe fruit of *Cathartocarpus fistula* (L.) Pers (*Cassia F.*—Pers.) (fam. *Leguminosæ*). The British Pharmacopœia defines this article, under the title *Cassiæ Pulpa,* as "the pulp obtained from the pods," this pulp being the only portion of the fruit used. The drug has been undoubtedly in use for five or six hundred years, but its name is much older, having been transferred to this substance from some variety of cinnamon to which it properly belonged. The tree is a native of tropical Asia, but is extensively cultivated for its beauty, both in the Old World and in the New. It is of medium size and produces long, drooping racemes of beautiful, showy, sweet-scented flowers.

The pods are nearly or quite straight, from thirty to sixty centimeters long by about 2.25 centimeters in diameter (12 to 24 in. by 1 in.), cylindrical, shortly stalked, and blunt-pointed. The surface is dark purplish-brown, and although not very smooth it has a dull polish. The dorsal and ventral sutures are marked by broad, flat, longitudinally striated bands running the length of the pod. The position of the partitions is generally noticeable upon the surface by means of shallow, annular constrictions about five or six millimeters ($\frac{1}{4}$ to $\frac{1}{3}$ in.) apart. The exocarp (shell) is hard and brittle when dry. The cavity is divided by transverse septa into from twenty-five to one hundred chambers, each containing one brown, shining, flattened seed and further filled with pulp. This last, when the pods are fresh, is soft and fills the entire space; as they dry it hardens into a thick, black, extract-like mass which eventually becomes hard and brittle and only covers the surfaces of the chambers, leaving the seed free and loose. When very dry, the quality is considered to be impaired. This pulp is removed for use by maceration. It has a sweetish, mawkish, mulberry-like taste and smell and is slightly laxative, but, at least in the dry state in which the fruits reach us, it has very little value. *Sugar, gum,* and other common vegetable substances are all that have been observed in it. Cassia Fistula is a traditional ingredient of the Confection of Senna. In the south of Europe it is more used. Dose: of the pulp, ʒ i. to iij. (4.0–12.0) as a laxative; as a cathartic, two or three times as much. The official confection contains ten per cent. each of senna and tamarind, seven per cent. of prune, twelve per cent. of fig, sixteen per cent. of cassia fistula, and one-half per cent. of oil of coriander, the rest sugar. The dose is ʒ i. to ij. (4.0–8.0). It is little used.

Henry H. Rusby.

Cassine.—*Black draught.* The leaves of *Ilex cassine* L. (Fam. *Ilicineæ*). These leaves, also known as Youpon, Dahoon, or North American tea, are the product of a large shrub or small tree that grows in great abundance in swamps and along streams near the coast of the southeastern United States. They contain about one-fourth of one per cent. of caffeine, on which account they constituted the basis of an important beverage of the North American Indians. The coast tribes consumed this drink habitually, while many of those of the interior made annual pilgrimages to the coast and, during their stay there, indulged in it to great excess. These leaves are therefore a practical equivalent of the Maté or Paraguay tea of South America. Besides the caffeine, the only constituent worthy of note is about seven per cent. of tannin. The article is now of little interest, except scientifically and historically. H. H. Rusby.

Castalian Springs.—Homes County, Mississippi.

Post-office.—Durant. Hotel.

Access.—These springs are located three miles west of Durant, at the point of intersection of the Y. and M. V. and Aberdeen branches of the Illinois Central Railroad, and about 250 miles north of the Gulf Coast. There are from ten to twelve passenger trains arriving at and leaving Durant daily, all of which are met by automobiles.

The country around the springs is generally rolling, with some high hills and beautiful valleys, making a charming combination. The location of the springs is about 300 feet above the sea level. Notwithstanding the great rainfall in this section, there is very little gloomy or cloudy weather. The clouds roll up quickly, discharge their contents, and disperse, leaving Old Sol to resume his sway. The temperature about the springs ranges, on an average, from 35° F. in winter to 65° F. in summer. The greatest extremes ever noticed are 10° F. the lowest, to 90° F. the highest. The place is used as a resort both summer and winter. The springs are situated in a pleasant little valley shaded by magnificent water-oaks, and surrounded by high hills with gradual slopes to the valley below. The hills are clad with evergreens of pine and some cedar. On the springs property which embraces some 360 acres, there are about fifty springs and wells, only two of which, however, have been analyzed or used for medicinal purposes. Of the following, one is a qualitative determination of the mineral ingredients, while the second is a quantitative one.

Spring No. 1.

(Examination by Prof. E. W. Hilgard, former State Geologist.)

One United States gallon contains 138.5 grains of solid matter, made up of the following ingredients in the order of their quantities:

Calcium sulphate.	Iron carbonate.
Aluminum sulphate.	Potassium sulphate.
Magnesium sulphate.	Sodium chloride.
Iron sulphate.	Silica.

Sulphureted hydrogen gas, strongly charged.
Carbonic acid gas, considerable quantities.

Professor Hilgard states that the waters may be classed as sulphureted-chalybeate. They possess the astringent qualities of alum water, while at the same time they have laxative properties from the presence of the sulphate of magnesium.

This spring yields about 600 gallons of water per hour, having a temperature of 56° F.

Spring No. 2.

(Prof. I. G. Patterson, State Chemist, Analyst.)

One United States Gallon Contains:

Solids.	Grains.
Calcium sulphate	37.23
Magnesium sulphate	15.18
Sodium sulphate	8.68
Silica	7.35
Ferric and aluminum oxide	4.84
Sodium chloride	2.47
Potassium sulphate	1.29
Total	77.04

This spring flows about 300 gallons per hour. The water is used for bathing purposes, and is also sold by the barrel or case. It has long held a wide reputation in Mississippi for the treatment of the malarial cachexia and for liver, stomach, bowel, kidney and skin affections. Emma E. Walker.

Castanea.—*Chestnut.* The leaves of *Castanea dentata* (Marshall) Borckh. (fam. *Fagaceæ*), collected in September or October, while still green. This is one of the largest and most valuable of our timber trees, growing rather rapidly, and producing an abundance of straight-grained, rather coarse, but very durable wood. The ripe fruit or nut is well known. The leaves are from six to ten inches (15 to 25 cm.) long, about two inches (5 cm.) wide, petiolate, oblong-lanceolate, acuminate, mucronate, feather-veined, sinuate-serrate, smooth, odor slight, taste somewhat astringent. Doubtless other species of chestnut leaves have the same composition and might with equal propriety be used. Nothing peculiar has been found among the constituents of chestnut leaves; nine per cent. of tannin, *resin*, and a number of mineral compounds in the ash, are the principal things observed.

Their use is entirely empirical. For a good many years they have had a popular reputation for the relief of whooping-cough, and within the last ten or fifteen years have been considerably used in its treatment by physicians; their value for this purpose is, to say the least, uncertain. Sometimes there appears to be a marked decrease in the number and severity of the coughing spells; at others no effect is produced. They are not put to any other use, although their powder has been largely employed for adulteration. The fluid extract is official, the dose being fl. ʒ ss.–ij. (2.0–8.0).

H. H. Rusby.

Castle Hot Springs.—Yavapai County, Arizona.

Post-office.—Hot Springs. Hotel and bungalows.

Access.—Via the Atchison, Topeka & Santa Fe and Southern Pacific Railroad systems to Ash Fork and Phoenix; thence via Sante Fe, Prescott & Phoenix Railway to Hot Springs Junction. Automobiles transport guests from Hot Springs Junction to Castle Hot Springs, a distance of twenty-four miles.

The resort is picturesquely and delightfully located in the foot-hills of the Bradshaw Mountains of Central Arizona, forty miles north of Phoenix and sixty miles south of Prescott. The climate is unsurpassed during the fall, winter, and spring months. The altitude is 1,971 feet. In this land of sunshine and blue sky a cloudy day is rarely seen. In January and February an average daily temperature of 70 degrees is common. The atmosphere is so clear and dry that dew and fog are unknown, and on account of the protection of the encircling mountains, this garden spot is immune from dust and winds. The scenery is unusually beautiful, mountain, canyon, and valley alternating in producing a remarkable panoramic effect. The vegetation of this region is nearly tropical. Scattered about the grounds are the date and other palms, the orange, grape-fruit, fig, and many other varieties of trees. Many beautiful song birds make their home here.

The following analysis of the Hot Springs water was made under the direction of the Department of Agriculture, Washington, D. C.:

One United States Gallon Contains:

Solids.	Grains.
Sodium sulphate	18.2
Potassium bicarbonate	1.1
Sodium bicarbonate	0.2
Alumina	Trace
Magnesia	Trace
Sodium chloride	12.9
Silica	3.5
Iron bicarbonate	0.7
Calcium bicarbonate	7.0
Lithia	Trace
Total	43.6
Reaction	Slightly alkaline.
Ammonia	None.
Nitrates	Trace.
Nitrites	None.

The water is mildly saline-alkaline-chalybeate, with a trace of lithia, and is remarkably free from organic matter or any other contamination. It is very palatable and large quantities may be drunk. There is a flow from the crevices in the solid granite, every twenty-four hours, of 400,000 gallons. The temperature of the water varies from 115 degrees to 122 degrees. Two recently constructed bath-houses are equipped with every facility for the application of the waters. There are at hand the spout, pool, vapor, Turkish, electric needle, Scotch douche, Schott Nauheim baths, and others. Swimming in the open pools of hot and cool water may be enjoyed any day in the year.

The hotel comprises three separate buildings and five bungalows. These structures are equipped with every modern convenience. The table is unexcelled. The hotel supports its own vegetable gardens and dairy. Golf, horse-back riding, trail walking, shooting, tennis, croquet, billiards, swimming, and other forms of recreation are at the command of the guests.

The environment is soothing to tired nerves and weary brains, the air being conducive to restful sleep. The water is efficacious in case of rheumatism and gout, anemia, bronchial catarrh, asthma, hay fever; in stomach and kidney affections, and in nervous disorders.

The season lasts from November fifteenth to May first. Emma E. Walker.

Castor.—*Castoreum.* The dried preputial follicles with their contents, obtained from the Beaver, *Castor fiber* Linn., and separated from the somewhat shorter and smaller oil sacs, which are frequently attached to them. The glands or reservoirs are usually connected in pairs by their excretory ducts, which open so near together as to be removed without dividing. They are oblong or pear-shaped, somewhat shriveled, multilocular bags, of dark-brown color (when dry) and tenacious consistence. The castor itself is within these; it is an unctuous brown or reddish-brown substance of intense and disagreeable smell. It consists of volatile *oil*, *castorin*, a *resinoid substance*, a peculiar fat, and other proximate principles, but like musk and others of its class the chemical composition is not especially instructive as to its qualities. There are two varieties of Castor, the Siberian, from the Siberian beaver, whose "pods" are longer (6 to 12 cm. = 2½ to 5 in.) and larger, and whose contents are more fragrant; and the Canadian, from the American variety. The latter is naturally the most common here.

This substance has been long used as a stimulant,

and antispasmodic in hysterical and other nervous conditions, but is now nearly obsolete as a medicine. It is no longer official either in this country or in Great Britain. There is some call for it as a basis of perfumes. Dose: gr. viij. to xxx. (0.5–2.0).

H. H. Rusby.

Castor Oil.—Oleum Ricini. "A fixed oil expressed from the seeds of *Ricinus communis* L. (fam. *Euphorbiaceæ*)." (U. S. P.) In temperate climates, this plant is an annual, often dying at the season's close without ripening its fruit; or, where the season is long enough, as in the Middle States, it bears abundantly the first year, and is killed by the approach of winter; but below the frost line, as in the extreme south of Europe, in Africa, and India, it becomes a shrubby or tree-like perennial, sometimes attaining, in the tropics, a height of forty feet. In the United States it usually attains a height of from three to twelve feet, with a round, very smooth, purple and glaucous, hollow, branching stem, and large, peltate or subpeltate, five- to eleven-lobed leaves. The flowers are borne in large, falsely axillary, paniculately branched spikes. The fruit is a short, blunt, prickly tricoccous capsule, containing three pendulous seeds. Castor-oil seeds vary considerably in size and markings; they are generally from one to two centimeters (about ½ in.) in length by about two-thirds as broad and half as thick, ovoid, blunt, and rounded at the ends. They are convex on the outer surface. The inner surface is usually flattened on each side of the middle by the pressure of the neighboring carpels, the two facets so formed uniting in a very blunt and rounded longitudinal angle. They have a good-sized

Fig. 1247.—Castor-oil Plant. (Baillon.)

caruncle at their upper end (or a scar if this has been broken off). The surface is very smooth and shining, usually of a gray color, marked with very pretty brown or blackish marblings. In color and markings, however, they may vary considerably. The nucleus consists of a soft, oily albumin, with a good-sized, straight, broad embryo in the middle. This plant is probably indigenous to India, but has been cultivated so long and extensively that its original home is difficult to determine. It has been completely naturalized, and grows with all the freedom of a native in other parts of Asia, as well as in many of the Mediterranean islands and coasts. It is cultivated extensively for its seeds in India, Southern Europe, and the Middle United States. It is a very variable species, and is divided into numerous varieties, mostly distinguished by the size, shape, and color of capsules or seeds.

The castor-oil plant was known to the ancient Egyptians and Greeks, and its oil was used for fuel, light, and medicine. It has even been suggested as the gourd that sheltered Jonah. After a long period of neglect, it was again brought into use, a hundred and twenty years ago, by Peter Canvane, a physician who had practised for many years in the West Indies, and who, in a treatise upon this oil, strongly recommended it as a gentle purgative (Pharmacographia).

The oil is separated from the seeds by the usual methods employed with fatty substances, viz., by boiling in water and skimming it off; by extracting it by means of some solvent like alcohol or ether; or by expression. The latter is the method employed in the United States. The seeds are carefully cleared from dust and fragments of the capsules, and then warmed, by which means the oil becomes more liquid. The mass is then subjected to strong pressure, and the expressed oil further purified either by standing and decantation or by boiling with water. The yield is about forty or fifty per cent. The purer the oil is, the less active and griping it is. If expressed cold from the peeled seeds, like the best Italian oils, it is very white and odorless, and almost tasteless.

Fig. 1248.—Seed of the Castor-oil Plant. Two-thirds Natural size.

The higher the temperature employed in the process, the greater is the tendency toward the freeing of the irritating and griping *ricinoleic acid*. The pulp left after expression contains a small amount of the albuminoid *ricin*, which is a powerful irritant and convulsive poison. This substance renders the action of the seeds so violent as to unfit them for use as a medicine, though the practice prevails in some countries of triturating one or two with a dose of the oil, to render the latter more effective.

Description.—The following is the official description: A pale yellowish or almost colorless, transparent, viscid liquid, having a faint, mild odor, and a bland, afterward slightly acrid, and generally offensive taste. Specific gravity: 0.950 to 0.970 at 15° C. (59° F.). Soluble in an equal volume of alcohol, and, in all proportions, in absolute alcohol, or in glacial acetic acid; also soluble, at 15° C. (59° F.), in three times its volume of a mixture of nineteen volumes of alcohol and 1 volume of water (absence of more than about five per cent. of *most other fixed oils*).

With an equal volume of benzin, it forms, at 15° C. (59° F.), a turbid mixture, but at 17° C. (62.6° F.) it yields a clear solution.

When exposed to the air in a thin layer, it slowly dries to a varnish-like film.

When cooled to 0° C. (32° F.) it becomes turbid, with the separation of crystalline flakes, and at about −18° C. (−0.4° F.) it congeals to a yellowish mass.

If 3 c.c. of the oil be shaken for a few minutes with 3 c.c. of carbon disulphide and 1 c.c. of sulphuric acid, the mixture should not acquire a blackish-brown color (absence of *many foreign oils*).

Castor oil consists almost wholly of a compound of *ricinoleic acid* ($C_{17}H_{32}[OH]COOH$) which is irritant and purgative when set free by saponification in the intestine.

Castor oil is a cathartic of very reliable character, more uniform and painless in its action, and more susceptible of gradation, than almost any other. The full dose clears the bowels with great certainty, producing numerous and copious discharges of their contents, with but little irritation of their surfaces;

indeed, when these are inflamed it appears to have a decidedly healing or soothing effect upon them. On these accounts, when the desire is simply to relieve the entire intestinal tract, either from the accumulated feces or from the irritating secretions of dysentery or enteritis, castor oil is the safest and surest means at the command of the physician. For attacks, also, of acute indigestion, and for the constipation following childbirth, it has long been almost universally used. It is not a hydragogue, nor is it very well adapted for continuous use in habitual constipation, although for "weak" and sensitive conditions of the bowels, when they are easily disturbed, now a little constipated, now a little loose, with frequent slight colics and flatulent tenderness, small daily doses of this medicine may be useful. Daily doses of ♏ xx. to xl., before breakfast, are recommended by high authority for overcoming chronic constipation. It is one of the ingredients of flexible collodion (*Collodium flexile*, U. S. P.), to which it gives softness and flexibility.

Administration.—There is scarcely a medicine in use which is generally taken with so much repugnance as this. When it can be taken clear this is the best way, or it may be mixed with syrup or glycerin, or floated upon the surface of some aromatic water, or in the froth of soda-water containing some aromatic syrup; or a regular emulsion may be made with it, such as is made with cod-liver oil, by means of mucilage or other emulsifying agent. But the taste of the oil usually outlives that of the added flavor, and these agents are, therefore, only partly successful. Another good way is to rinse the mouth with clear whiskey or other spirit, or lemon juice, then immediately to swallow the oil, and follow it with another rinsing with the liquor. If thoroughly emulsified, with the addition of orange juice, a confection is formed which is almost unobjectionable. Finally, it is put in elastic capsules, which for small doses, in the case of patients who will learn to swallow them, completely cover the taste. All these means, however, are more adapted to grown persons than children; for these the emulsion is probably the best, or it may be covered with a little lemon juice or glycerin. Another useful way to give castor oil, in certain cases, is by injection; in this way it acts principally locally and mechanically as a lubricant, but a certain quantity must be absorbed, as there is often more result from it than would be explained in this way. A good method is to give, for an adult, from 60 to 120 grams (℥ ij. to iv.) clear, to leave it for from one quarter to three quarters of an hour in the bowel, and then to follow with a full enema of soap and water. Very free emptying of the lower bowel usually follows.

Castor oil is absorbed to a slight extent by the skin, but the method has no practical value.

Dose by the mouth as a laxative, from ℥ i. to iij. (4.0–12.0), as a purgative, ℥ ss.–i. (15.0–30.0). Children require large proportionate doses. A baby a week old can easily bear ♏ xlv–lxxv (3.0–5.0), and a child of five or six years, ℥ ij–iv (8.0–16.0).

Henry H. Rusby.

Castration.—Strictly speaking, castration means only the ablation of one or both testicles, or orchidectomy, although medical writers frequently extend the term to include removal of the ovaries as well. In this article the original meaning of removal of the male organs is retained, and for a description of the operation in the female the reader is referred to the title *Ovariotomy*. For the effects, both mental and physical, of removal of the testicles or ovaries in the young, see *Genital Glands, Effects of Removal of the*.

Anatomy.—A few anatomical studies of certain of the parts involved under this heading would seem appropriate. Their more direct bearing will subsequently appear.

There are three *arteries* which convey blood along the spermatic cord: the spermatic, the cremasteric, the artery of the vas deferens.

The *veins* comprise two chief groups, an anterior and a posterior, but as a whole are known as the pampiniform plexus, which empties, by a single vein, upon the right side into the ascending vena cava, upon the left into the left renal vein.

The *lymphatics* of the scrotum and its contents empty in three ways: Those of the scrotum, including the parietal layer of the tunica vaginalis, end in the superficial inguinal lymph nodes. Those of the testicle, epididymis, and visceral layer of the tunica vaginalis empty in the juxta-aortic lymph nodes. Those from the vas deferens end in the external iliac lymph nodes. From the testicle the lymphatic vessels pass up along the cord through the inguinal canal, and accompany the spermatic vessels until near their ending in the juxta-aortic glands.

The *vas deferens*, which averages two feet in length, after accompanying the cord through the inguinal canal, parts company from the other components of it at a point but little deeper than the deep abdominal (hernial) ring. It now curves around the outer side of the internal epigastric vessels, crosses the external iliac vessels, and at once dips down into the small pelvis, accompanying the bladder to its base, crossing the obliterated hypogastric artery, and passing to the inner side alike of the ureter and of the seminal vesicle of its own side.

Its lumen is but half a line; its walls exceedingly thick relatively. Were excision of even several inches of it to be performed with the fallacious idea that thereby, when done upon both sides, a result could be obtained, as effective against procreation in habitual criminals as that following double castration, the attempt would fail if subsequently the criminal should engage the services of a surgeon equally adept and at the same time unscrupulous. The ends freshened and joined over a half inch or so of double O catgut rigid from alcohol, which is inserted like a mandril—if need be, first carefully stretching the caliber by a round needle—could be retained by three or four finest silk or linen sutures. It has at the hands of various surgeons been successfully performed, following accidental division of the vas during operation for radical cure of inguinal hernia with old adhesions between cord and sac.

Technique of Simple Castration.—*Step* 1: Make an incision upon the anterior surface of the scrotum downward from the region of the superficial abdominal ring—which lies just above the pubic spine. This guide (the spine) is easily to be felt at the lower end of Poupart's ligament. The length of this cut depends upon the size of the sarcocele (chronic enlargement of the testis) demanding its removal. It is to be long enough to permit delivery of the testis by pressure from below aided by traction upon its cord from above.

Step 2.—Using dry gauze dissection, free the cord just below the superficial ring aforesaid, so that the finger may be passed about the cord.

Step 3.—Deliver the testis; tie off the cord very firmly, preferably with Wallaby tendon (so-called Kangaroo tendon) too strong to break from steady tension. By means of such very tight constriction the sensory nerve fibrils included are rendered incapable of conveying the sensation of pain, to any severe degree.

Step 4.—Amputate the cord at a point a full inch below the ligature—to avoid any possibility of its slipping off of the stump.

Step 5.—Transfix both pillars of the superficial ring and the cord between them, passing through, at two levels, using Wallaby tendon as a suture mate-

rial. Thus we make sure that the cord may not with time slip up through the ring and thus render at least more possible the advent of an inguinal hernia.

Castration for Malignant Disease.—To have any hope against recurrence it is as essential here as in cancer of the breast, to be radical, removing the diseased tissues *en masse* so far as possible, and following up the limes of lymphatic drainage, removing these and all tangible lymph nodes—as will presently be mentioned more in detail. Of course this remark applies to carcinoma, not sarcoma, since the latter does not spread along the lymphatic system, but through the blood-vessels.

Step 1: Make a liberal incision from a point near the anterior-superior spine of the ileum down to one opposite the superficial ring, or much lower, upon the scrotum even if large size of growth demand such length of cut. This incision runs parallel to Poupart's ligament and an inch about it.

Step 2: Much as if for Bassini's hernia operation we next deepen the wound, splitting the fibers of the external oblique—here an aponeurosis, not a muscle—and then exposing the spermatic cord.

Step 3: By dry gauge dissection free the cord from end to end of the superficial cut. To do this toward the outer end necessarily involves cutting the internal oblique and transversalis muscles.

Step 4: Ligate—preferably with Wallaby tendon—the cord, except the vas, at as high a point as practicable—somewhere near the anterior-superior spine. Clamp an inch below the ligature and divide.

Step 5: Follow the vas as far down toward the lower pelvis as is thought practicable. Ligate twice and divide between. Cauterize by aid of a needle thoroughly by carbolic acid the lumen distal to the ligature upon the stump. Simply to divide the vas, without these added precautions, may well lead to escape of semen from above into the absorbing tissues—semen containing cancerous cells and secretions, or tubercle bacilli when the disease under treatment is of the latter nature.

Step 6: Deliver the cancerous testicle (assuming this not greatly enlarged) through the superficial wound as described, wholly by traction from above. Do not squeeze nor otherwise handle it from below further than is compulsory. To be sure, by means of the ligation of the cord already done we have taken precaution against our chief line of danger from such handling. There remains, however, the lymphatic connection with the scrotum proper, and where, at least, distinct adhesions are noticeable, this is a real risk.

Assuming that in one or several *quite small* spots the cancerous organ is adherent to the scrotal skin; perhaps, too, in the midst of such adhesions, especially in long-standing malignant disease, fistulæ exist, leading into the testis proper. Such cases are best handled at operation as follows: Supplanting step 6—aforesaid, let us lightly curette each fistula, thus removing detritus, granulations from about its mouth, etc., and then pack it firmly with a slender strip of gauze or of narrow tape, dampened in tincture of iodine. Let this also be applied to the (necessarily) adherent skin surrounding each fistula. Next, by scalpel, we incise the normal skin about each small adhesion with or without a fistula in its midst; following the shape of the adhesion, with our knife, but at a distance a half inch or more away from any apparent disease, and deepening into the sac of the tunica vaginalis.

Step 7: Now would come the delivery, by traction in the cord, upward into the large wound described as step 1—of cancerous testis plus adhesions and packed fistulæ. By our precautions, as specified, it is likely that the wound, during this almost momentary contact would not be contaminated. However, immediate irrigation should follow, plus a coat of tincture of iodine painted upon the raw surfaces.

Where adhesions are large, between skin and testis, it is doubtless best, instead of step 6—to ablate this entire half of the scrotum, carrying down our primary cut like an inverted capital Λ, and surrounding everything diseased. Then Step 7 as described can be carried out, as before, by traction from above, not aided by squeezing or handling from below, and entirely open work, since one long cut runs from the region of the anterior-superior spine of the ileum to the bottom of the scrotum.

Where any adhesion has existed between testicle and scrotal coverings we must remember that the skin, the parietal layer of the tunica vaginalis, and the several fascial layers between drain their lymphatics through the superficial inguinal lymph nodes. Therefore Step 7 would include our doing as thorough a removal of all distinguishable glands in this region as possible. While our primary wound is yet open, too, let us remember to search where the vas deferens crosses the external iliac vessels for any enlarged nodes there—which is where its lymphatics empty. And so far as we can run backward along the deep course of the spermatic vessels let us search for and remove any lymph nodes. Indeed, in a bad case, it would be only good surgery to advocate opening the belly by a separate median incision, exposing the lower end of the aorta, upon either side of which lie the juxta-aortic glands, requiring removal as being the emptying place of the lymphatics belonging to testis, epididymis, and visceral layer of the tunica vaginalis.

Of course the closing of the great primary wound constitutes *Step* 8, and this is of especial interest because offering an ideal opportunity to prevent the occurrence of inguinal hernia upon this side. The entire absence, now, of any spermatic cord obviates the need of two rings and the inguinal canal joining them; structures which must not be permitted to fit the cord so closely as to pinch; and this comfortably loose fit to a certain degree invites a loop of the thin gut to slip down alongside. This is why—recognizing the indubitable fact that if we render the belly wall solid here, as much so as at any level higher up, we safeguard against inguinal hernia's return as nothing else can do—many surgeons especially during the middle ages used to castrate, and ablate the cord, too, as a regular part of attempted radical cure of inguinal rupture. At that time the belief was general that one testicle supplied male semen, the other female ditto; though there was no unanimity of opinion as to which side was responsible for a given sex. And it is a fact that at one time a law was promulgated and enforced by one of the potentates of a German principality, prohibiting castration for this purpose, lest in consequence soldiers who otherwise might be born for their country's defense be replaced by girls.

The modern technique in suturing for radical cure is so nearly perfection, by whichever of several well-known methods we operate, that the results nearly approach the best that castration could give us; and now nobody takes this surgical step because of hernia.

In closing the wound we unite the conjoined muscle of the internal oblique and transversalis to the deep, shelving portion of Poupart's ligament, and then the split external oblique aponeurosis is united, either edge to edge, or preferably overlapping for added strength, if absence of spermatic cord gives slackness of the parts enough to permit this. All such sutures the present writer prefers to have of Wallaby tendon, and interrupted. The skin may be closed in any accustomed way. If much dry, gauze dissection has been needed, or if there is the least doubt as to the asepsis of the wound, it is well to provide drainage for from a day to several days, according to how quickly

the dressings become soiled. A dressing should never be allowed to remain in contact with a wound long enough to become saturated. The moment this happens it has become useless, and the blood begins to absorb the poisons from the wound, which it is the function of the dressings to drain away outdoors by capillary action.

Dry gauze sponge dissection is a great factor in safety where adhesions exist, to important structures—but its employment instead of the sharp edge leads to a free exudation of serum into the wound. This, if the wound be closed, forms a splendid food for any chance microbes, inviting them to multiply until they swarm in a few hours. Also, by holding the normal, living flesh planes apart and preventing prompt adhesion and solidification of the wound structures, such dead serum does harm. When only the sharp edge has been employed we have afterward a comparatively dry wound. In such case, and when we believe the work to have been aseptic throughout, it is best to close our wound without drainage. A light coat of tincture of iodine, even in such a case, seems a wise measure of precaution, and is applied just before the closing.

Epididymectomy.—Sarcocele when of tuberculous origin almost always first invades the epididymis. In time the testicle proper may alco become involved; and given time enough, extension up the vas and into the seminal vesicle of the same side may eventuate. Formerly it was thought essential to ablate the testis with its epididymis and all the vas possible, when this disease of the epididymis had been diagnosticated. To-day we recognize that far less radical measures suffice; that is that König's opinion with that of Kocher and others is now superseded by the views of J. B. Murphy, Tillaux and various recent operators, who speak in the light of their results after leaving the testis proper in the scrotum in such cases. Murphy considers epididymectomy counterindicated in the following three conditions: (1) Such tuberculous disease elsewhere as must soon necessarily be fatal; (2) when the body of the testicle is riddled with the disease, here castration, entire, is indicated; (3) where numerous scrotal tuberculous sinuses exist. Aside from these three conditions he advocates resection—removal of epididymis and vas, leaving testis. And it must not be forgotten, in favor of this view, that the presence in the economy of the testis, even without the epididymis, has in some way a useful influence over metabolism. Murphy has also pointed out that after double removal of the epididymis "sexual desire and potency, even to emissions, are retained; power of procreation, however, is lost."

In many cases even where plain evidence exists of tuberculous involvement of vas, seminal vesicle, and even of the bladder, epididymectomy has sufficed to effect in time a cure; nor can we feel surprised that this is so. Differing strikingly from the clinical facts of true malignant disease, where leaving any tissue involved means ultimate death, we all know that in various surgical fields less radical measures suffice, often, in the case of tuberculosis. For the most striking example we may cite tubercular peritonitis, where the mere opening of the belly so commonly proves curvative. Then the partial removal of tuberculous glands, with absorption of the smaller ones, occasionally left through need of speed in operating is a case in point; again the commonest major excision —that of the knee for tubercular involvement—would if really radically attacked, take an hour or more of careful dissection; whereas certain surgeons habitually rely upon removal of the worst of the disease depending upon nature for the rest. It is a risky omission upon the operator's part, and certainly not one to be emulated where time and strength of patient justify more radical work. However, it deserves mention herewith as a remarkable phenomenon which under the present heading has often been followed by cures formerly thought most unlikely.

Technique of Epididymectomy.—Step 1: Begin by an incision through the outer side of the scrotum, toward its rear part, vertical and parallel with the epididymis. If any fistulæ or adhesions are present, excise these and remove them *en masse* with the diseased epididymis.

Step 2: With the knife follow down the line between testis and epididymis, from the same (the outer) side. This cuts into the tunica vaginalis along the main part of the organs, but above, in clearing the globus major, we necessarily cut the tunica albuginea, and at the globus minor again the same covering. In separating testis from epididymis be careful upon their inner junction, because there is the line of entrance and exit of the spermatic vessels. The work just here is best done by gauze sponge dissection, until the vessels are clear to the view. Be cautious to divide none needlessly, for the nutrition of the testicle proper remains to be considered and provided for.

Step 3: Any foci of disease in the testis which may now come into view should be excised by wedge-shaped cuts, and the edges apposed with catgut or linen. Likewise close off the incisions made in the tunica albuginea.

Step 4: Follow up the vas to a high point—say the level of the deep inguinal ring, at least; ligate and cauterize its lumen distal to this ligature upon the stump. For safeguard it seeems best to ligate with non-absorbable material rather than even chromic catgut, lest finally the vas become again patent. The technique of the cauterizing has been described earlier in this article.

Step 5 is, of course, the wound closure, which presents nothing different from that discussed under castration for malignancy—except that the bulk of the spermatic cord being retained, we cannot make quite so absolute a certainty against any future advent of hernia. Robert H. M. Dawbarn.

Casts, Urinary.—See *Urine*.

Catalase.—This belongs to the group of oxidizing enzymes, the oxidases, its particular activity being the liberation of oxygen from hydrogen peroxide. This enzyme is very widespread and so is generally obtained together with other enzymes when organ or tissue extracts are made. It is a matter of speculation just what function catalase plays in the animal organism. Its distribution is different for different organs of the same animal, but remarkably constant for the same organ in the same species. In general, the order of decreasing strength is: liver, kidney, blood, spleen, gastroenteric mucosa, salivary glands, lung, pancreas, testicle, heart, muscle, brain. In embryos catalase is scanty, but increases rapidly after birth. In various pathological conditions catalase is said to be reduced. Frank. P. Underhill.

Catalepsy.—This term (from κατά, down, and λαμβάνειν, to seize) denotes a psychomotor condition, characterized by a peculiarly increased tonus of the muscles, which though rigidly contracted, yield to external force, so that the limbs can be moulded, as it were like wax ("flexibilitas cerea") and can be made to assume strained attitudes, which they then preserve for some time against the force of gravity. At the same time there is clouding of consciousness, more or less profound, with impairment, to loss of cutaneous sensibility. It was formerly thought that fatiguability was entirely in abeyance in this condition, but more accurate methods of observation and recording have shown that after a time there are unmistakable signs of fatigue, the raised arm, for instance, tending gradually to sink

and compensatory movements adapted to bring other muscle groups to the assistance of the tiring muscles occurring, while strain is evidenced by irregularity and increased frequency of respiration. It cannot be denied, however, that in some cases these signs are a long time in appearing. Consciousness is nearly always impaired, though probably often not as completely lost as it would seem. Binswanger indeed asserts that in hysterical catalepsy there is inhibition, but no loss of consciousness and the patient can tell later what happened while he was cataleptic. In the severe and protracted cases, the respiration is slow and shallow, the heart's action is weakened and the vital functions are depressed, the condition resembling that of trance, in which latter, however, muscular rigidity is not a feature. With the condition of extreme abstraction known as ecstasy, catalepsy has also some points in common. While formerly described as a functional nervous disease, catalepsy is now considered only a symptom.

The origin of the name reflects the ancient view that the cataleptic attack was due to the sudden seizure of the victim by some supernatural influence, as an evil spirit, while the causes to which it has been assigned, even by medical writers, are varied in the extreme and many of them absurd. A number of classical examples of catalepsy could be quoted from the literature of all times and its close relationship with the ecstatic and trance-like conditions so frequently indulged in by the mystics of all ages has already been touched upon. It has been observed in connection with a number of nervous diseases, both functional and organic, but a specially fertile soil for its development is found in the extreme suggestibility of hysteria. That it occurred regularly as a phase in the attack of grand hysteria was clearly brought out by Charcot and the Paris School; and since on account of the greater care exercised by physicians in avoiding suggestion, grand hysteria is now rarely seen, hysterical catalepsy has correspondingly decreased. To the same authorities we owe the demonstration of the possibility of inducing cataleptic phenomena as a stage in profound hypnotism. These facts furnish a ready explanation of the frequency of catalepsy in the subjects of intense religious fervor. Catalepsy has been observed in epilepsy, in chronic alcoholism, and in various organic diseases of the brain, as tumors, hydrocephalus, abscess, and general paresis, while a special form of "cerebellar catalepsy," in which the patient lies in the dorsal recumbent position, with partial flexion and abduction, with rigidity of the lower extremities, has been described by Babinski. Partial and hemicatalepsy have also been observed. The condition to which, however, catalepsy has come of recent years to be specially attached, and of which it is considered a symptom par excellence, is that variety of the insanity of adolescence or dementia præcox known as catatonia (*q.v.*). In this disease it is associated with gradually progressive dementia, with episodes of excitement, depression, and stupor, often not in its complete form, but as varying degrees of waxy rigidity with other peculiar motor manifestations. Attempts to explain the phenomena of catalepsy have so far not been successful. Since it seems closely related to certain hysterical manifestations, the dissociation between the higher and lower cerebral centers, with disturbance in the coordination of the mental and motor processes and lowered or suspended inhibition, predicated for hysteria, may with some plausibility be assumed to be the psychopathological basis of catalepsy, but here we are dealing with theories only.

Since catalepsy as a symptom is characteristic, *diagnosis* concerns itself chiefly as to what is the underlying condition and our principal concern is in determining whether this is a functional or an organic disease. Its *prognosis* rests upon similar grounds. While a symptom of grave impairment of the cerebral processes and, where there is no organic disease, suggestive of a severe neurosis, or of a psychosis of probably unfavorable outcome, catalepsy in itself does not usually imperil life, though patients have died in cataleptic attacks. Where the stupor (or inhibition) is of long duration, refusal of food and impairment of nutrition may become a menace.

Treatment.—In hysterical cases, by strong counter-irritant measures such as dashing water in the face, inhalation of ammonia, or the production of nausea by the hypodermic injection of apomorphine, it may be attempted to cut short the attack. It is hardly necessary to say that such measures have no place in cases of organic disease, or in catatonia. In the occasional cases which last days or weeks, it is necessary to see that the bladder and bowels are emptied at regular intervals and that the patient is properly nourished, by tube feeding, if necessary. Otherwise the treatment is that of the underlying disease.

Charles Lewis Allen.

Catamenia.—See *Menstruation.*

Cataphoresis.—A term employed to express certain phenomena that occur when a current of electricity is passed through solutions of various salts. Under such conditions the salts are separated into their elements, certain being attracted to the positive pole and other to the negative. If a membrane separates two solutions the same exchange takes place and the terms *electric-osmosis* and *electric-diffusion* have been applied. Recent advances in chemical science and the clearer conception of the theory of *ions* has simplified the explanation of this process. We now recognize that not the elementary molecules, but molecules in the more stable state of ions, are attracted to the different poles and preserve their characteristic action.

As a therapeutic measure this action has been taken advantage of for the purpose of conveying remedies from the surface of the body, through the unbroken skin, to the deeper tissues. The salt is applied to the epidermis and a current of electricity is passed through it, one pole being placed over the drug and the other at some remote part. This is now generally known as *ionic medication* (*q.v.*).

Beaumont Small.

Cataplasma Kaolini.—This is the only cataplasma or poultice official in the United States Pharmacopœia. Kaolin is a fine white clay, composed chiefly of pure aluminum silicate, but containing also small quantities of aluminum hydroxide, ferric oxide, magnesium oxide, and calcium carbonate. *Cataplasma Kaolini* (U. S. P.), Cataplasm of Kaolin, contains kaolin 577, boric acid 45, thymol, 0.5, methyl salicylate 2, oil of peppermint 0.5, and glycerine 375. It is used as a cleanly poultice in the place of the more or less filthy poultices of flaxseed, bread and milk, etc., which were formerly in vogue, and which were all that could be desired for the multiplication of bacteria. The cataplasm should be heated and applied in a thin layer and then covered with cotton or lint.

R. J. E. Scott.

Cataract.—Definition.—Strictly speaking, cataract may be defined as any pathological condition of the lens marked by visible opacities. For practical purposes, however, the term is enlarged to cover certain anomalies of the lens, in which there is a considerable diminution of vision, without the presence of definite opacity. No sharp division between this condition and that in which definite opacities are present is possible.

Cataract was recognized by the ancient Greeks

and Romans, but they had an erroneous conception of the disease, in that they supposed the opacity to be upon the lens rather than in it. They believed that it was caused by the pouring out of an opaque fluid between the iris and the lens, and since it was supposed that this fluid was poured down from above, it attained the name, "Cataracta" (cataract). The real nature of cataract was demonstrated by a Frenchman, Brisseau, in 1705. His views, when presented to the French Academy, were at first scorned, and were not accepted until some three years later.

Situation.—Cataract may be situated in the lens or in its capsule; hence, we have lenticular cataract, capsular cataract, and a combination of the two, capsulo-lenticular cataract.

Subjective Symptoms.—The subjective symptoms of cataract are not characteristic. Patients usually complain of failing vision, of seeing through a fog or veil, or of seeing black spots or lines, which change their location only on movement of the eye, and always occupy the same relative position (in contradistinction to vitreous opacities). Occasionally, multiple vision (polyopia) on looking at bright points of light, such as a star, the moon, or a street lamp, is noticed. This difficulty is caused by the irregular astigmatism produced in the lens by the developing opacities, and may occur before actual lenticular opacity can be demonstrated.

Another not uncommon feature is the development of myopia. The patient begins to see distant objects better through a concave glass. If beyond middle life, he may lay aside his reading glasses, or even require a weak concave glass for the purpose. This change constitutes the so-called "second sight" of those advanced in years, and though it does not occur invariably in cataract development, it is sufficiently common to be a diagnostic feature of some importance.

The degree of visual disturbance is dependent both upon the character and upon the seat of the opacity rather than upon its extent. So long as an opacity, even if extensive, is confined to the equatorial region, that is, so long as it lies completely behind the iris, vision may be affected little or not at all; but when the pupillary area is invaded, the vision immediately diminishes, especially when the opacity is diffuse, in which case the lens may be compared to a window-pane covered with watery vapor. When the opacity is sharply circumscribed, vision is less involved, and this condition may be likened to a clear pane of glass covered by a netting or by a wire screen. If the opacity does not occupy the whole of the pupillary area, the degree of visual acuity depends on the size of the pupil and on the illumination. Patients with a central opacity of the lens see best with the moderate illumination of a dark day, before sunrise and after sunset, as the pupil is larger then than when the light is bright. Consequently, in such cases, the use of a mydriatic is often advisable to eke out and prolong vision, which is being reduced from this cause. The reverse is true when the opacity is in the periphery. The patient sees best with a bright light, and dilatation of the pupil, which exposes the diseased portion of the lens, disturbs the vision to a considerable extent. An opacity of given size causes more disturbance at the posterior pole of the lens than at the anterior pole, for near the posterior pole lies the nodal point of the eye, through which all rays of light, which do not undergo refraction, must pass. As the opacity in the lens increases, the patient becomes blind. He can no longer see objects (qualitative vision), but he still retains the perception of light (quantitative vision). The examination of this last named function is of great importance, for it tells us the condition of the retina and optic nerve, and whether an operation is indicated.

Objective Symptoms.—Far advanced opacities in the pupillary area of the lens may be recognized by the naked eye, as whitish or grayish discolorations. All cases should, however, be examined by lateral focal illumination, and by means of the ophthalmoscope, and for a thorough examination, dilatation of the pupil with a mydriatic, such as homatropine, is indispensable. The tension of the eyeball should, however, first be carefully noted. For the examination with lateral illumination some form of loupe, and especially the Czapski binocular corneal microscope, is useful. The lenticular opacities appear as gray or white spots, or striæ. Anterior capsular opacities may be distinguished by their whitish color and prominent situation.

By transmitted light with the ophthalmoscope, lenticular opacities present a grayish-black to black color, and stand out in contrast to the red reflex of the pupil. Opacities assume an extraordinary number of forms, the most common of which are the radially situated sector-like opacities which show the close connection of the progress of the disease with the original lines of development of the lens. If a concave mirror be used in the ophthalmoscope, the illumination obtained may be too bright to show up very slight opacities; consequently, a plane mirror and moderate illumination should also be employed. For the recognition of fine opacities, a strong convex lens may be useful. In this examination, the eye of the observer should be closely approximated to that of the patient, so that the lens is at the focus of the convex glass.

By lateral illumination, the seat of the opacity may be usually ascertained. More accurate in some ways, however, is the estimation, by means of the ophthalmoscope, of the amount and direction of the paralactic movements.

It should be remembered that the lens in advanced age always possesses a large nucleus, which reflects more light than does the non-sclerosed lens of youth. This explains the grayish reflex observed in the pupillary area of old people, and consequently no diagnosis of cataract should be made without the employment of the above-mentioned methods of examination.

Pathology.—In capsular cataract, the lens capsule divides and forms a convex surface posteriorly, almost entirely composed of several layers of epithelial cells. Anteriorly, the cells are fewer, take on a spindle shape, and may even be absent in the very forward parts. Between the two layers is a mass of homogeneous fibers, irregularly disposed, and containing few nuclei. Calcareous deposits may occur in the latter stages of the disease.

In lenticular cataract, various changes occur, according to the type of opacity, to its situation, and to the stage of its development. It is manifestly not within the scope of this article to describe the changes which have been found in all forms of lenticular cataract. In general, they are as follows:

Changes in the capsule are rarely absent. In the lens, the fibers separate and leave spaces which soon become filled with fluid in the form of small droplets of fat. The fibers then swell and may become irregular in outline. As they swell they become opaque and numerous fine droplets appear. As the lens fibers break down, the connection between them and the capsule becomes loosened. Degeneration goes on, and finally, the place of the fibers is taken by a pultaceous mass. If a nucleus is present it is open to doubt as to how much it takes part in the general process. That it is usually comparatively free from change, is the belief of Hess.[1] In his text-book Fuchs states that in exceptional cases the nucleus and not the cortex may be the first part to become opaque in the lenses of adults. Elschnig[2] is of the opinion that changes in the nucleus are much more common.

Clinical Forms of Cataract.—These are many, and in their classification many points must be considered. As yet, no thoroughly satisfactory classification has been propounded. In this article the writer proposes to follow in a general way the arrangement given by Fuchs.

We may first divide them into stationary cataracts, where an opacity has developed at some point in the lens, and has remained permanently limited to that spot, and into the progressive form, where the opacity has increased, until the whole lens has become involved.

Anterior-polar Cataract.—To the partial stationary cataract belongs the anterior-polar variety. This is a small, sharply defined, white spot at the anterior pole of the lens. (Fig. 1250.) The congenital form of anterior-polar cataract is due to a failure in the development of the lens. The acquired form results from the perforation of a corneal ulcer, as in gonorrheal ophthalmia of the new-born, producing contact between the diseased corneal tissue and the anterior pole of the lens, and causing degeneration; later, there is proliferation of the capsular epithelium, through the action of toxins. Acquired anterior-polar cataracts are larger than the congenital, but seldom in themselves give rise to any essential visual disturbance.

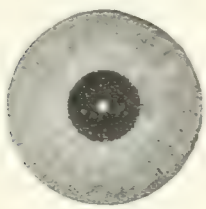

Fig. 1250.—Anterior-polar Cataract. (After Bach in Axenfeld's Lehrbuch.)

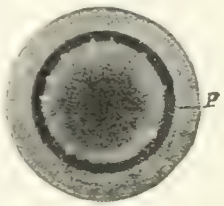

Fig. 1251.—Perinuclear or Zonular Cataract with "Riders," seen by Reflected Light. (After Bach in Axenfeld's Lehrbuch.)

Posterior-polar cataract is a small white dot, situated at the posterior pole of the lens. It is of congenital origin, and is due to the incomplete disappearance of the hyaloid artery, which, in fetal life, runs through the vitreous to the posterior surface of the lens. It causes no noticeable disturbance in vision.

Of the rare, partial, stationary cataracts belonging to the lens proper, central cataract, fusiform, or spindle cataract, and punctate cataract may be mentioned.

Lamellar Cataract (Perinuclear, Zonular).—This is the form of cataract most frequently seen in children; but exceptionally, it may come on in later life. It consists in an opacity, lying between the nuclear and the cortical layers of the lens. Seen by lateral illumination, it appears like an opaque or partially opaque nucleus to an otherwise transparent lens. Closer examination reveals its center to be transparent. Occasionally, two distinct zones of opacity are seen. The peripheral portions of the lens are usually clear. Along the outer edge of the opacity may often be seen small radially-situated opacities, riding anteriorly and posteriorly over the circular zone, and consequently known as riders. The diameter of the zone of opacification is very variable. It may be as small as three millimeters, or as great as eight millimeters. In almost all cases, both eyes are affected. The opacity develops congenitally or shortly after birth. Children with rickets and with the tetany of childhood are especially affected. By many it is regarded as an anomaly of development, and numerous instances of inheritance have been recorded.

Lamellar cataract is usually stationary, but may develop into a total opacity. The visual disturbance is chiefly dependent on the density of the opacity, and varies between almost normal sight and a considerable diminution in vision. This form of cataract is not always characterized by the above-described appearances. Various forms of dots and figures may often be seen in the anterior and posterior portions of the lens.

Treatment depends on the amount of vision. If an arbitrary line must be drawn, it may be said that anything less than twenty-fiftieths requires operation. In some cases, where a broad zone of lens periphery is clear, an optical iridectomy will produce a considerable improvement in the sight. This may be ascertained by dilating the pupil, and seeing whether an improvement in vision occurs. Removal of the cataract is the usual operation performed, and in children, by means of repeated needlings and absorption. Later on in life, extraction is indicated.

Both of these procedures, iridectomy and extraction, have their definite indications. If iridectomy is chosen, the opacity itself is not attacked, and vision is always somewhat defective. The eye is disfigured and the pupil enlarged. If the cataract is removed, the patient is dependent on glasses and loses his power of accommodation. Even when cases of congenital amblyopia are excluded, the results of treatment are often exceedingly bad. One of the most fruitful causes of failure, especially in children, is the attempt to operate without an anesthetic.

It is admitted that even under most favorable conditions a vision of better than one-third of normal cannot be obtained by iridectomy, and this is insufficient for many trades and professions. For this reason and others, Kuhnt[3] thinks iridectomy should be reserved for exceptional cases. The indications are to remove the lens, leaving the pupil intact. Adhesions of the iris should be avoided. Every precaution should be taken to avoid future diminution in the vision obtained by operation. In three to five per cent. of cases, the pupil does not dilate properly, and iridectomy should be performed upward. The first needling should be a trying-out operation, and should be made cautiously. Kuhnt is opposed to primary extraction of lamellar cataract, as the risks are too great. After the first needling, it is best either to wait, or to perform a second needling, or to do a linear extraction when the lens is completely opaque. Every effort must be taken to prevent the development of after cataract; and the younger the patient, the more liable is this to occur. To avoid nystagmus, Kuhnt[3] believes that the operation should be done early in life, even in the first few weeks; while Hess sees no objection to waiting until the child is two or three years old.

Anterior- and posterior-cortical cataracts form a connecting link between the non-progressive and progressive forms of cataract. In the anterior- or posterior-cortical layers of the lens, a stellate opacity is seen with a more or less opaque center, and rays extending out to the periphery. The posterior-cortical form is more common than is the anterior. This cataract occurs in connection with diseases of the deeper parts of the eye, and represents a constitutional disturbance. The opacity usually remains stationary for many years, and then may progress to total cataract formation. It has, however, been known to clear up (Fuchs), showing that the opacity may be simply a swelling of the lens fibers. On account of the other pathological changes in the eye, the prognosis for vision after an operation is bad.

Progressive Cataract.—This begins with the appearance of slight opacities, developing either in the periphery or in the center of the lens, and progressing in youth until the whole lens becomes opaque. This is, however, not the case in later life, for a portion of the lens nucleus is already sclerosed and usually does not take part in the opacification.

Elschnig[5] takes exception to this view, however, and as a result of his studies has come to the conclu-

sion that senile cataract is, as a rule, a total cataract; that is, the nucleus and cortical layers become opaque, and deviations from this rule form relatively infrequent exceptions.

The rapidity with which opacification takes place varies widely in different cases. Exceptionally, total cataract has formed in a few hours, while in many instances a number of years intervene.

In the development of cataract, four stages may be distinguished, which are best marked in the simple senile cataract, the commonest form.

Incipient Cataract.—Ordinarily, a few opaque striæ appear in the periphery of the lens radially arranged. Their appearance is always to be regarded as suspicious, but does not necessarily mean an advancing cataract, as the increase may be exceedingly slow. Thus, until we find evidence of a considerable increase in the opacity, it is best not to frighten the patient by a positive diagnosis of disease, since it is easily possible that vision may remain good for some years to come. For our own protection, it may be best to warn a relative of the patient as to the condition.

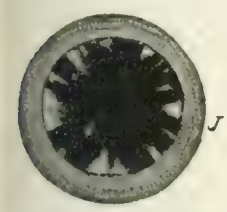

Fig. 1252.—Incipient Subcapsular Senile Cataract, as Seen by Reflected Light. The iris (J) has been retracted by atropine. (After Bach.)

Intumescent Cataract.—As cataract formation continues, the lens imbibes water and swells, the opacity increases, vision fails and the anterior chamber becomes shallow. The degree of advance of the opacification toward the anterior capsule may be determined by means of oblique illumination. If some lenticular tissue in this region is still transparent, the iris will throw a shadow of itself in the pupillary space. The amount of transparent substance may be estimated by the depth of the shadow. In cataracts that are nuclear in origin, swelling of the lens from imbibition does not occur.

The duration of the stage of intumescence may last several months to years.

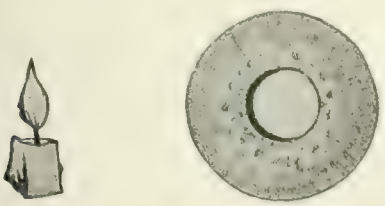

Fig. 1253.—Immature Subcapsular Senile Cataract, Seen by Reflected Light. The crescentic shadow is seen on the side of the papillary edge on which is the light. (Bach in Axenfeld's Lehrbuch.)

Mature Cataract.—As the opacification continues, the lens loses the fluid it has taken up and becomes totally opaque, and vision is reduced to the seeing of hand movements or to the perception of light. The anterior chamber regains its normal depth. The lens loses the shining bluish reflex it usually exhibits during the stage of swelling, and becomes a dull grayish-white. The connection with its capsule is loosened by degeneration of the lens fibers in contact with it.

In a cataract which has advanced so that the deeper parts of the eye cannot be seen, how shall we know that the case is suitable for operation? This can be told by the examination for the perception and projection of light. The patient is seated in a dark room and directed to look straight forward. The examiner, standing twenty feet away, holds a lighted candle and moves it to various portions of the visual field. The patient should be able to distinguish the direction of the light if the eye is healthy. For practical purposes, it is easier to make this examination in connection with the other examinations made with artificial light. The source of light is reduced to equal that of the candle at twenty feet, and it is reflected with the mirror of the ophthalmoscope into the patient's eye from all directions.

Hypermature Cataract.—This is the fourth or final stage. Cortical masses disintegrate and become fluid, the lens takes on a milky appearance, and its structure can no longer be made out. The nucleus, which is more resistant to degeneration, may sink to the bottom of the capsule and present itself there as a brownish shadow, changing its position with movements of the head, the so-called *Morgagnian cataract.* Not infrequently, the cells of the anterior capsule proliferate, and appear as irregular whitish opacities. Further change in the broken-down lens tissue may occur by the absorption of the fluid, thus leaving a membranous mass in which lime salts or cholesterin may be deposited. The zonula of Zinn may become atrophic, so that a trembling of the lens and iris is observed during the movements of the eye. Hypermature cataract is characterized also by the abnormal depth of the anterior chamber.

Black Cataract or Cataracta Nigra.—In some old people, sclerosis of the lens may advance so far that almost the whole lens becomes transformed into nucleus. By lateral illumination, a brownish reflex is clearly visible, and although it may be possible to obtain a satisfactory view of the fundus with the ophthalmoscope, vision is very considerably diminished. Extraction of the lens is indicated in these cases, and a generous corneal section must be made to allow for a lens of unusual size.

Etiology.—The cause of cataract has not, as yet, been established with certainty, although many theories have been advanced.

Congenital cataract is probably due either to disturbances in development of the lens, or to intrauterine inflammation. The influence of heredity is often seen. Heredity has also a certain influence in senile cataract, as there are many records of families particularly predisposed to this disease. Age alone will not suffice as an explanation, or all old people would show lenticular opacities. It is a pathological rather than a physiological change. To make a diagnosis of senile cataract, one must exclude all those diseases in which cataract occurs.

Becker's theory, which found many supporters, suggested that the sclerosing of the nucleus, when it does not progress uniformly to the formation of a black cataract, offers a hindrance to the diffusion of nourishing fluid throughout the lens, and shrinking of the nucleus occurs, which leads to a loosening between the nucleus and its immediately enclosing layers; the spaces formed become filled with fluid, followed by opacification and degeneration of the fibers. The determining moment for this nuclear change, Becker, however, lays to changes in the general organism.

Von Michel believed that atheroma of the carotid bore an intimate relationship to the causation of cataract.

Peters looked for the cause in the disturbance of the equilibrium between the tissues of the lens and the aqueous. For the proper nutrition of the lens, a higher molecular concentration is necessary than that of the aqueous. This relationship must be retained by the capsule epithelium. Degenerative changes in the epithelium of the ciliary body, as described by various writers, lead to an increased concentration of the aqueous, with consequent decreased diffusion of substances into the lens and deficient nutrition, leading to the changes known as cataract formation.

A more probable explanation, and the one which best sotisfies, comes from the observations of Hess on experimental cataract. The first change which can be observed pathologically consists in a more or less

extensive degeneration of the epithelium of the anterior capsule. The whole theory presupposes general organic changes, the formation of injurious substances, which, when reaching the capsule, cause its degeneration followed by the later degeneration of the lens fibers.

Römer regards senile cataract as due to the action of specific cytotoxins. Under normal conditions, the secretory organs of the eye are sufficient to protect against the action of these substances, but when an excess of these substances is present in the blood serum nad they find their way into the aqueous, they penetrate the lens capsule and possess a special affinity for the protoplasm of the lens fibers.

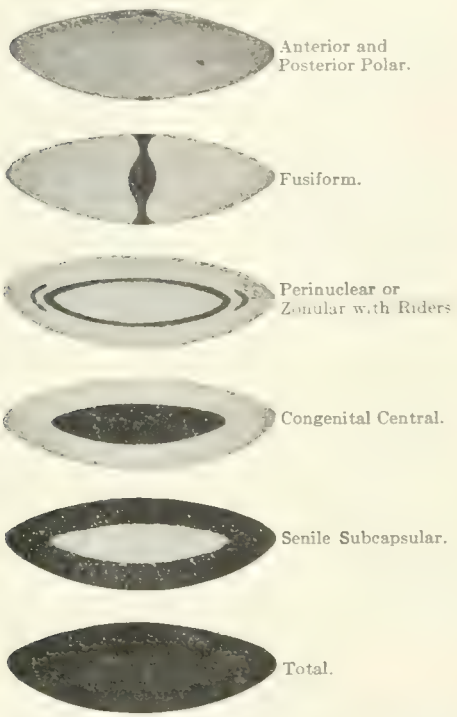

FIG. 1254.—Schematic Representation of the Areas of Opacity (Shown in Black) in the Different Varieties of Cataract. (After Bach in Axenfeld's Lehrbuch.)

That senile cataract is caused by some condition existing in the system at large is practically certain. It always affects both eyes, though usually at different times, and if the eyes show any evidence of disease, the more diseased eye becomes first affected.

Von Graefe first made the observation that the prognosis after operation is better in the second eye than the first.

Cataract in General Disease.—Diabetic cataract is the most frequent of these forms. It is bilateral, and not infrequently develops in comparatively young individuals and in those whose urine shows a high content of sugar. Diabetic cataract may develop in a comparatively few days. Formerly, it was believed to be due to the abstraction of water from the lens, but more recently it has been shown that the amount of sugar contained in the aqueous is too small to produce opacity of the lens, and consequently we must assume a more complicated action.

The prognosis for operation is less favorable than is that of senile cataract, on account of the diminished resistance to infection and the greater predisposition to iritis. Consequently, before operating the glycosuria should be reduced by treatment as much as possible. In this connection, it may be noted that beginning opacities of the lens, not too far advanced, have been known to disappear in part under strict diet and general treatment.

Cataract is also observed in naphthalin poisoning, ergotism, pellagra, tetany, cholera, and in connection with disease of the thyroid gland.

In glassblowers, cataract occurs relatively often, and begins around the fortieth year. Only the part of the lens unprotected by the iris is affected, and the cataract is more apt to develop on the left side than on the right, as this is the side which they turn toward the molten glass. Its exact causation is, as yet, unknown.

Lightning may cause cataract, as well as strong electric shocks, by the power of strong electric currents to kill living cells.

Hess has produced experimental death of the lens epithelium by electric shocks.

Traumatic Cataract.—Any injury which produces an opening in the lens capsule is followed by cataract formation. Such an injury may occur from a punctured wound, from the penetration of some foreign substance, or from an operation. Contusions of the eye can produce rupture of the capsule. Concussion of the lens may be followed by opacification even without rupture of the capsule.

Traumatic cataract is due to the admission of either aqueous or vitreous into the lens, followed by swelling and opacification. A few hours after injury the lens in the neighborhood of the capsular wound is seen to be opaque, and later the swollen tissue projects from the wound and gathers in flocculi in the anterior chamber. The extent of the process may vary from a very slight and localized opacity—due to early closure of the wound—to a total absorption of the lens.

The size of the wound naturally has much influence on the amount of final injury, as does the age of the patient, for in youth swelling takes place much more quickly and is much more extensive than later in life.

Increase of tension not infrequently occurs from swelling of the lens. It need not lead to serious consequences, although operative interference, by either puncture into the anterior chamber, removal of the lens, or iridectomy, may be necessary in order to reduce the hypertension. Inflammation from traumatism of the uvea or from infection is an unfavorable sign in traumatic cataract, and may lead to adhesions of the iris to the lens, which renders later extraction of the cataract difficult, or it may even lead to destruction of the eyeball.

Complicated Cataract.—Under this heading, we class those lenticular opacities which are due to other diseases of the eyeball. Either the nutrition of the lens is disturbed, or it is injured by the access of toxic substances. Complicated cataract may occur in disease of the uveal tract. It very frequently does occur in connection with retinal separation, absolute glaucoma, intraocular tumors, high myopia, retinitis pigmentosa, etc. In appearance, there may be no marks to distinguish it from other forms of cataract, or it may present characteristic features, such as stellate opacities in the anterior or posterior cortical layers or regressive changes, such as thickening of the capsule, the deposition of lime salts or cholesterin, or by liquefaction. In all cases, a careful examination of the ocular functions should be made, for in complicated cataract the perception and projection of light are usually faulty.

Experimental Cataract.—This may be produced by the administration of naphthalin to rabbits, and has been observed in humans after the use of naphthol ointments on the skin. When the aqueous is evacuated, it is possible to produce cataract by massage of the cornea with a blunt instrument. Cataract has also been produced by electric shocks, and by exposure for a considerable time to intense light.

Medical Treatment. In view of the great advances made in the diagnosis and treatment of diseases of the eye during the present generation, as well as of the earnest efforts that are still being made in all directions to further ophthalmological science, it would indeed be hazardous to assume that no local application or general medication to affect the progress of cataract will ever be discovered. None the less, it must be firmly asserted that, at the present day, we possess no means whatever of preventing this disease. Numberless remedies have been tried in the past, but have all proved inefficacious, and at the present day none but charlatans assert their ability to cure cataract without an operation. Some administer nostrums, others make topical applications, while others again extol the virtues of electricity; the result in every instance being the same. If the cases of reported cure be thoroughly sifted, it will be found that by far the larger proportion are based on a mistaken diagnosis; that in many instances the process has simply come to a standstill.

Surgical Treatment.—This consists in reopening a path for the rays of light to reach the retina, either by the side of the existing obstruction (iridectomy) or by its absolute removal. The latter may be affected in one of three ways: The cataract may be left in the eye, but be pushed aside from the axis of vision (reclination, depression); it may be caused to undergo absorption by being brought in direct contact with the aqueous humor (discission); or it may be bodily removed from the eye through an opening made for the purpose (extraction).

General Considerations.—The indication for an operation for cataract is a probable improvement in vision. (In certain cases, operation is indicated for cosmetic reasons.) The two preliminary questions, therefore, to be settled are: first, as to whether a careful examination of the condition and functions of the eye renders it likely that the cataract can be successfully removed; and second, whether the general health is likely to be injuriously affected by the excitement attending the operation, or the subsequent confinement that is necessary.

As a rule, it is undesirable to operate on a teething child, a pregnant woman, or one who is menstruating or about to do so. The general condition of the patient should be carefully inquired into, and the prognosis modified if any general disease like diabetes or Bright's disease is present and it is yet deemed desirable to proceed with the operation.

If the patient is fresh from a journey, a rest of a day or two should be allowed. If the operation takes place away from home, a sufficient time should be afforded the individual to familiarize himself with his new surroundings.

On the continent of Europe, there is quite a general agreement among the ophthalmic surgeons that serious operations, like the extraction of cataract, which entail a lengthened convalescence, should be performed away from home; generally in the private rooms attached to the hospital with which the surgeon happens to be connected. An establishment especially arranged for the purpose offers advantages of light, ventilation, quiet, and skilled attendance, with which no ordinary private house can compete. There is, moreover, a freedom from care and anxiety that can rarely be secured at home. For the first day or two, relations and friends being excluded, there can be no allusion to exciting topics or consultation on household cares. Distance from the latter is found to induce, with the head of a family, a feeling of repose that close proximity would go far to destroy.

Should one eye be operated on when the other is entirely normal? Assuming the cataract to have been removed sucessfully, there are certain undeniable advantages in the association of such an eye with a normal one. Although the lens is wanting, and the refraction of the two eyes thus radically different, the patient has a larger visual field than if he had only one eye, a better estimation of distance, and appreciation of solidity. He is no longer blind on one side, and when moving about, avoids accidents to which he would otherwise be liable. Although such an eye cannot even be fitted with the proper convex glass, it forms a reserve, and can instantly be brought into use if anything happens to the unoperated eye. Furthermore, if we wait until the vision of the second eye is poor, we may be forced into a difficult operation on a hypermature cataract. A cataract is most favorable for extraction when it is ripe, and so long as the vision of the patient's good eye is sufficient to enable him to carry on his occupation, maturity should be waited for. If, however, sufficient vision in the better eye is lacking, it is better to proceed and extract the immature cataract.

The modern views on this point differ from the older ones, since it was shown by Hirschberg and Schweigger that in general between the fiftieth and sixtieth year, and certainly after the sixtieth year, most cataracts could be completely removed even if they do not present the classical signs of maturity. The great stress that was laid on waiting for maturity, in the preaseptic times, had its grounds chiefly in the liability to infection, and consequently surgical intervention was deferred until there was a reasonable chance that one operation would be sufficient. Modern asepsis has so lessened the dangers of secondary operations that this point of view no longer holds.

Patients are sometimes encouraged by their home advisers to wait until both eyes are fully affected, in order that both may be operated on at the same time. While the simpler cataract operations may undoubtedly, under ordinary circumstances, be performed in the young on each eye at one time without incurring unwarrantable risk, the extraction of senile cataract on both eyes simultaneously is unjustifiable, save in the most exceptional cases. And this for the following reasons: If one eye only be operated on, the symptoms which follow, and the way and manner in which the eye rallies from, or, in extreme cases, sinks under, the violence inflicted on it, guide us materially in what we are to do for the other eye, and teach us to adopt such precautions, or so to modify our method, as to give the patient a better chance of sight and to save him from the dangers to which our ignorance of his idiosyncrasies exposed him in the first instance. Again, a patient or his attendants, being little used to such delicate operations, may be imprudent, transgress our positive directions, and consequently lose the eye. If both eyes have been operated on, his only chance is gone. If, however, one only has been touched, he will learn wisdom with experience, and insure success by being more careful the second time.

It is true that the refusal of the surgeon to operate on both eyes at the same time often practically results in but a single operation being performed. After the confinement of a fortnight in a darkened room, the average patient may well shrink from a repetition of his experience, or fear its effect on the general health. Many people have not the time to give to the second operation, or the means of meeting its attendant expense. These are, however, minor considerations, and are not to be weighed in the balance with those which have been brought forward to show the superior safety of operating on but one eye at a time, in all cases of senile cataract.

Preoperative Technique.—A general examination of the patient should be made to determine, if possible, the cause of the disease, and secondly to ascertain if there is any obstacle in the way of recovery. The presence of glycosuria or albuminuria need not be a bar to operation, unless one or the other present in marked degree, in which case operation should be

postponed and treatment should be carried out to get the patient in the best possible condition.

In obtaining the history, it is well to seek for information as to the behavior of the patient at any previous operation, since in the extraction of cataract so much depends on this. In the same way, his reaction to drugs, and especially to solutions of atropine, should be noted, as a considerable proportion of individuals suffer from belladonna irritation. The nervous condition of the patient should be investigated with a view to combating possible mental derangement after operation.

As absolute relaxation must be obtained after cataract extraction, any tendency to cough may prove troublesome or dangerous, and should be controlled before operation. The nasopharynx should invariably be investigated, and in the event of any affection being present, operation should be postponed.

As a rule, the patient should enter the hospital the day before operation, and means should be taken to clear the intestinal tract. A careful examination should be made to ascertain if any infection of the lid borders exists, and even if the conjunctiva looks normal and is free from pathological secretion, it is good practice to make smears and cultures to guard against the presence of an abnormal number of the bacteria which are commonly found, and especially to see that the pneumococcus is absent. The tear passages too should be investigated and proved normal, for it is in pathological conditions of this apparatus that the pneumococcus is most prevalent. Where lacrymal obstruction is present, extirpation of the sac should be practised as the only safe measure, since it has been shown that the former procedures—cauterization and tying off the puncta—are insufficient. It has also been shown that the conjunctiva becomes relatively safe within a few weeks after extirpation of the sac. No definite time limit may be given, but each case must be judged by the appearance and by the result of bacteriological examination.

Local preparation of the eye should be preceded by a general bath, and if necessary, cleansing of the hair, which in women should be confined by some sort of cloth head dress or rubber cap. The usefulness of a trial bandage on the eye, is doubtful.

The skin of the eyelids and around the eye should be thoroughly scrubbed on the morning of the operation with gauze and green soap, and mopped off with some antiseptic solution such as alcohol or bichloride of mercury. The field of operation should then be covered with sterile gauze and a bandage until the time of operation.

Just before the operation, the eyelashes should be cleansed by rubbing with a sterile swab and soap and water. Von Pflugk, however, denies the efficacy of this procedure, and recommends the use of a swab over which twenty drops of benzine have been poured. A considerable number of operators trim the eyelashes before operation. It is well known that it is impossible to render the conjunctival sac completely sterile, and that the use of strong antiseptics produces a condition of irritation which is favorable to the growth of microorganisms. Therefore, irrigation of the sac should be performed with little force, and some bland fluid, such as sterile boric acid or physiological salt solution, should be used from an undine or from a jar connected by a tube and nozzle. The field of operation should be walled off by suitable arrangements of towels and gauze.

Little need be said as to the preparation of the operator. What holds for general surgery, is equally applicable here. He should wear a mask, and in an operation of this kind where delicacy of touch is essential, rubber gloves should not be worn. To make up for the loss of protection which they afford, the operator and his assistants should see that the part of an instrument or swab which they grasp should not come into contact with the field of operation.

All solutions to be used in connection with the operation should be boiled. Solutions of cocaine of four per cent. and higher may be boiled with impunity. Instruments are best sterilized by boiling in a weak alkaline solution (such as sodium hydrate or carbonate one per cent.), though some surgeons prefer the use of dry heat.

To Daviel is awarded the honor of having introduced the modern method for the extraction of cataract. Up to 1750, when he decided to remove all cataracts by this method, reclination of the lens was the operation almost universally practised, and from then on well into the nineteenth century it was a contest between reclination and extraction, with many supporters on each side.

Percival Pott, in 1775, one of the strong supporters of reclination, made use of a fact which he discovered during that operation; that if the capsule of cataracts not easily depressed were freely opened, absorption of the lens took place through action of the aqueous. This operation proved successful when confined to the cataracts of young children and young adults, but met with failure when applied to hard cataracts.

Daviel's operation was performed with an instrument not unlike the modern keratome. The incision was made at the lower margin of the cornea, and enlarged upward on each side with a blunt-pointed knife or scissors until it included half the cornea. The flap was then raised with the spatula still in use, and known as Daviel's spoon, and the lens was incised with a sharp needle. The lens was then forced out by pressure of the fingers applied on the lower lid.

Sharp, in 1753, was the first surgeon to make use of a single knife in making the corneal section, and following him, many forms of knives were invented. Before the end of the eighteenth century, the knife had generally superseded the instruments of Daviel.

In the preaseptic days, Jacobson came to the conclusion that incisions situated in the scleral tissue were less likely to suppurate than those in the cornea, also that scleral incisions healed more quickly. It was with this in mind that von Graefe perfected his linear extraction of cataract. What he wished to secure was a linear wound with a scleral position, and as this could not be accomplished with the lance-shaped knife which was then being used, he invented a new form of knife with a long thin blade, modelling it after the iris knife of Waldau and Froebelius. In all essentials, this is the cataract knife in use at present.

Incisions for cataract were as numerous, and varied as much as the knives. Only the more important ones will be alluded to. Von Graefe's idea was to make an incision that would as nearly as possible be an arc of the largest possible circle. Puncture and counterpuncture were made one millimeter from the cornea and one and one-half millimeter below a tangent drawn through the summit of the corneal circumference. As this incision proved too small, it was later lengthened and combined with an iridectomy and a small conjunctival flap. This method was called the combined linear extraction, in contradistinction to the simple linear extraction without iridectomy.

For many years, this incision was practised, and it was only finally given up because it was found that although cases of severe infection were less frequent the incision was hard to make, that large lenses were difficult to extract, and that iris prolapse, loss of vitreous and cystoid scars were frequent. Little by little the details of the operation were modified until the flap operations of the present day were evolved.

Although at the present time there are many methods of extraction differing as to detail, they may be divided into three general classes: simple extraction (without iridectomy), combined extraction (with iridectomy) and extraction of the cataract in the unruptured capsule.

Technique of Cataract Extraction.—Some special form of operating chair or table is used by many surgeons, but in general it may be said that any good operating table will serve, or the patient may be operated on in a bed which is wheeled into the operating room and back into the ward or room after operation. This latter procedure allows for the least possible exertion of the patient. On the other hand, the patient may be allowed to walk to the operating room, and after the operation to be carried to his bed in some of the various forms of stretcher. Some operators even go so far as to allow the patient to walk back to bed, and then examine the eye to see if any prolapse has occurred.

It is well for the operator to be present when the patient is placed on the table in order to quiet his fears and to give a few necessary instructions, including a short drill in moving the eyes in various directions. He should be told that the operation is nearly painless if he follows directions and avoids squeezing up his lids. The eye is anesthetized with four or five applications of a four-per-cent. solution of cocaine although some prefer holocain in a one-per-cent. or two-per-cent. solution. It is well also to instill a drop in the second eye.

As to the condition of the pupil at the time of operation, there is still much difference of opinion. Some prefer a contracted pupil on the ground that the knife is less likely to engage in the iris and that there is less tendency to prolapse of the iris after simple extraction; while others argue that prolapse is even more likely to occur on account of the barrier the iris forms against the flow of fluid into the anterior chamber; furthermore, that under certain circumstances it is much more difficult to deliver a large, hard nucleus through a contracted pupil, and that masses of cortical material are likely to be retained behind the iris.

On these grounds, Hess prefers to secure maximum dilatation of the pupil before performing a simple extraction; while in the cases where iridectomy is to be performed, he contracts the pupil, believing that under those circumstances it is possible to do a smaller iridectomy than could otherwise be secured. It should be stated that the dilated pupil shows a very considerable degree of contraction after escape of the aqueous. Many operators employ neither a miotic nor a mydriatic before the operation.

The eye having been anesthetized, the speculum is introduced by first engaging the upper lid and then the lower. While the spring speculum is generally used to-day, not a few prefer to control the lids by means of lid elevators held by the assistant, on the ground that there is less pressure on the eyeball and that the spring speculum is less easily removed in an emergency. It is well to use a speculum having some form of guard which obviates the possibility of instruments coming in contact with the lashes, and which thus reduces the liability to infection.

In cataract of the right eye, the operator stands at the patient's head; while if the left eye is to be operated on, custom varies. The surgeon may either stand at the patient's head and use his left hand, to which one soon becomes accustomed, or he may stand or sit in front of the patient and cut away from himself.

The knife is grasped between the thumb, index- and middle fingers, so that its axis is almost at right angles to the axis of the fingers. The fixation forceps is held in the left hand and a fold of conjunctiva, as close to the limbus as possible, is grasped at the lower inner quadrant of the eyeball. Some operators secure fixation by a grasp of the internal or of the superior rectus.

The patient is directed to look down, and the operator having steadied his hand by resting the little finger against the patient's forehead, the point of the knife is introduced at the limbus one and one-half millimeters above the horizontal meridian of the cornea. The point of the knife is carried somewhat backward until it appears in the anterior chamber. It is then carried directly across, and a counterpuncture is made at a point which corresponds to the point of puncture. With a long, steady, sawing motion, the knife is then made to cut upward in a plane parallel to the plane of the base of the cornea. As the upper point of the incision is reached, care is taken not to complete the incision too rapidly, a procedure which might cause prolapse of the iris. The knife is then turned upward and backward, and a conjunctival flap of suitable size is made. The conjunctival flap is now reflected down over the cornea with the knife or spatula. The corneal flap is raised and a drop of cocaine allowed to come in contact with the surface of the iris. In most cases, at this point the fixation forceps may be removed. If not, they may be handed over to an assistant.

If an iridectomy is to be performed, the iris scissors (the writer prefers De Wecker's) are grasped in the right hand, while the iris forceps, held in the left, is introduced closed between the lips of the wound almost to the pupillary border of the iris. The blades are then opened, and a fold of iris is grasped and drawn through the wound. As a small iridectomy will suffice, it may be best obtained by a single closure of the scissor blades directed at right angles to the incision. The patient may be warned that at this point he may experience slight pain.

In former times, the cystitome was used almost entirely for opening the lens capsule, and with many operators it is still in favor at the present day.

If the iridectomy has been performed, the cystitome with the straight shaft may be introduced into the anterior chamber. In simple extraction, it is necessary, however, to bend the shaft of the instrument to a very considerable angle. It should be carried into the eye with its cutting edge turned backward in order to avoid any injury of the iris. From the temporal side, it is carried across the anterior chamber and introduced slightly under the nasal edge of the iris. The blade is then turned, and a curved incision through the capsule made by drawing the instrument toward the temporal side. If a larger opening be desired, this incision may be connected with a vertical incision running upward from the lower edge of the pupil.

In 1880, proposals were made by several operators to remove the largest possible piece of capsule by means of specially designed forceps, and since that time the use of capsule forceps has steadily increased until now it is the instrument of choice of a large number of operators.

Capsule forceps should be introduced closed through the wound and carried across the anterior chamber almost to the opposite margin of the iris. The blades should then be opened, pressed backward to grasp the lens, and closed. The first movement should then be downward toward the patient's feet in order to tear the capsule at the upper part of the lens. The closed forceps is then withdrawn from the eye. If, after closing the forceps, the first movement is upward, there is more likelihood of leaving a tag of capsule between the lips of the wound. It is wise to float the bit of capsule off the forceps in whatever sterile fluid is at hand in order to see that a piece has been removed.

The lens is now ready for extraction. If the patient be restless, or if there is reason to suppose that the vitreous is fluid, it is best to remove the speculum and to control the lids by means of elevators. In any case, if the speculum be left in, it should be supported by the assistant and not allowed to exert any pressure on the eyeball. The lens spoon is grasped in the right hand, and the spatula in the left. The eye may be rotated downward, unless loss of vitreous is feared. In this case, there is less danger

if the patient is allowed to look forward, or even upward. Steady pressure toward the center of the globe is now made with the spoon at the lower margin of the cornea. As the lens appears at the wound, the direction of the pressure may be changed to somewhat upward. As the lens passes through the wound, the amount of pressure applied must be greatly diminished, in order that no vitreous be forced out. The spoon is then passed gently over the surface of the cornea in order to remove as much of the cortical substance as possible.

Irrigation of the anterior chamber, in order to obtain as complete an extraction as possible, has recently been extensively used, but seems to be losing favor somewhat at present. Hess believes that it may be dispensed with, and advises the introduction of a shovel-formed instrument into the anterior chamber. With this he supports the vitreous, while massage with the Daviel spoon or a specially curved instrument is made over the surface of the cornea to evacuate as much of the cortical substance as is possible. When the pupil appears clear and black, it is best not to make further efforts.

The toilet of the wound is next performed. With the spatula, the iris is freed from the angles of the wound and replaced in its normal position. All clots and shreds of capsule should be removed from the wound by means of forceps. When the margins of the wound are in position, the conjunctival flap should be stroked upward. The sac may be flushed out with a few drops of salt solution. A drop of atropine or eserine may be applied, according to the custom of the operator. The lids are closed, and the edges are best covered with some form of non-irritating, sterile ointment, such as White's ointment,* which contains a small amount of bichloride of mercury, or even with sterile vaseline. The eyes are then covered with a double pad, and the hollows are filled in with a suitable amount of absorbent cotton. This dressing may be secured with three or four strips of plaster reaching from the forehead to the cheek. A tie bandage may be used, or a roller bandage, or some form of wire, aluminum, or pasteboard protectors. The eyes should certainly be protected at night from the involuntary movements of the patient by the use of some stiff mask which will obviate the possibility of the wound being opened by any undue pressure from the outside.

The patient is then removed to his bed, and should be directed to lie as quietly as possible for the first twenty-four hours. An attendant should be constantly within reach to see that he makes no exertion of any kind. It is immaterial whether the room be light or dark.

As to the first dressing, custom varies somewhat, but ordinarily the eye is inspected within forty-eight hours after the operation. It is best to change the dressing at the end of twenty-four hours, but the eye need not be opened if there is no pain or evidence of any complication. At each dressing a drop of sterile one-per-cent. solution of atropine is instilled. Both eyes are ordinarily kept bandaged from three to five days, while the operated eye should be bandaged for from six to eight days. The patient may be allowed to have a bed-rest in from twenty-four to forty-eight hours, while at the end of three or four days he may step from his bed into a chair.

After the bandage is removed, dark glasses are worn and the eye carefully protected from too much light. In from eleven to fifteen days, the patient may go to his home; and six weeks after the operation glasses may be fitted.

Combined Versus Simple Extraction.—Each case should be judged on its own merits. The chief complications of simple extraction are prolapse of the iris, which in some statistics reach from ten to twenty per cent., and which may be followed by uveitis, astigmatism, or an irregular pupil. Moreover, in simple extraction a larger incision is required to deliver the lens, and greater difficulty is experienced in its removal. Cortical matter more frequently remains, producing secondary cataract. Greater skill is also needed on the part of the operator.

The advantages of simple extraction are cosmetic and optical, while there is also less likelihood of vitreous prolapse.

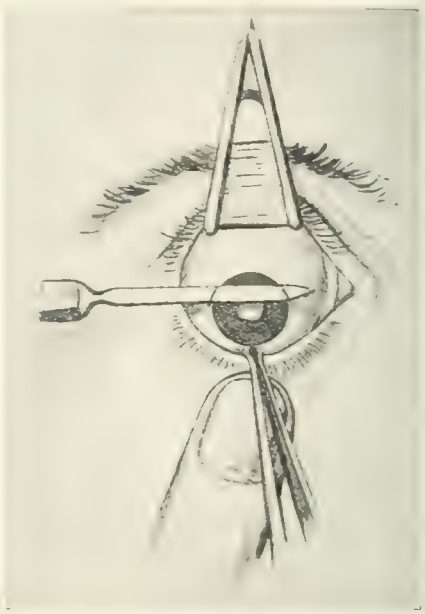

Fig. 1255.—Incision in the Flap Operation for Senile Cataract. (After Bach in Axenfeld's Lehrbuch.)

The combined operation is the more conservative procedure, and should, in the writer's opinion, be performed in the majority of cases, reserving simple extraction for those where the cosmetic feature is of great importance, where the iris dilates easily and shows no tendency to prolapse, and most important of all, where the patient has absolute control of himself during the operation. A few operators still perform a preliminary iridectomy a few weeks or days previous to extraction.

In 1890, Chandler first proposed to reduce the percentage of iris prolapse in simple extraction by incising the root of the iris with the knife. He later modified this by making a small buttonhole opening in the iris periphery after the lens had been extracted. To do this, the iris is seized at its root by small forceps with teeth at the end. It is drawn out of the wound, and a very small piece is excised with a thin-bladed scissors.

In 1904, Chandler published a series of 312 cases in which four prolapses occurred, and two of these were due to direct violence.

Schweigger and Bajardi proposed a similar procedure a few years later, and this has been adopted in more recent times by Hess.

Accidents During Operation.—After making the puncture, the knife may penetrate the iris. If the aqueous has not already been evacuated, the point of the knife may be withdrawn from the iris in most cases without much difficulty.

The iris may fall in front of the knife as the section is being made. If an iridectomy is planned, it is best to proceed with the operation; whereas, if the reverse be true, the knife should be withdrawn and the operation postponed until a later day.

* White's ointment causes irritation in a small number of cases.

The knife may be introduced with the cutting edge in the wrong direction. When this occurs, it is often possible to rotate the knife in the wound; otherwise, the knife must be withdrawn and the operation postponed.

The most common accident is the loss of vitreous. This may occur at any point during the operation, and may be due to muscular contraction on the part of the patient, to the operator, or to the condition of the eye itself. If vitreous escapes before the lens has been extracted, it is necessary to introduce a wire loop or a metal scoop behind the lens for its withdrawal. Prolapse of the vitreous is less to be feared after removal of the lens. However, it renders the replacement of the iris more difficult, and allows of a faulty coaptation of the wound edges. Infection is also more likely to occur. If a single drop of vitreous presents itself or escapes, it is best to lift it up with forceps and excise it close to the incision. Where a large amount is lost, the speculum should be immediately removed, and the eye closed, as an attempt to cut off the vitreous or replace the iris would only lead to further disaster. Loss of vitreous is to be avoided, although it is not necessarily a very serious complication. Healing is delayed in these cases, and the eye is more likely to be irritable for some time.

Subsequent complications may also take place, such as floating vitreous opacities, connective-tissue bands in the vitreous, and detachment of the retina. In uncomplicated cases of extraction, the corneal wound closes within a few hours, and the cornea itself is clear except for a slight opacity at the margin of the cut.

Where a conjunctival flap has been made, this region is much reddened for a few days. In some cases the eye may be absolutely white at the end of a week, while in others it shows considerable irritation.

Not infrequently, quite fine lines or stripes are seen in the deeper layers of the cornea running at right angles to the wound, the so-called striped keratitis. This is due to folding of the deeper layers and of Descemet's membrane. It disappears in the course of two or three weeks.

Reopening of the wound, through coughing, sneezing, etc., after it has closed not infrequently takes place, and need not be serious.

Prolapse of the iris is comparatively frequent in simple extraction. It is best to etherize the patient and excise the prolapse as soon as possible. Cauterization of the prolapse has been practised, but is warned against by Gifford, who considers that this procedure is not infrequently followed by sympathetic inflammation. If the prolapse be left untouched, infection may occur months or years afterward.

Vitreous prolapse is seen less frequently after simple extraction than after the combined. It is more common, however, in the extraction of the lens in capsule.

Delayed healing of the corneal wound may take place, and union may not occur for several weeks after the operation. In these cases, it is not necessary to retain the bandage, for it is not unusual for healing to occur shortly after the bandage is removed. Separation of the choroid occasionally occurs after cataract extraction. Attention was first called to it by Fuchs. With the ophthalmoscope a dark, rounded mass is seen projecting forward in the region of the ciliary body and anterior part of the choroid. It is due to tearing of the attachments of the ciliary body and root of the iris, so that fluid penetrates between these structures and the sclera. It may appear immediately after the operation, or as much as a month later. This complication need not cause anxiety, as healing invariably takes place, although it may be delayed for several weeks.

Not infrequently glaucoma is seen after cataract extraction. In most of the cases, it follows an inflammation of the iris complicated with posterior synechiæ. It is also not uncommon where the corners of the iris or the lens capsule are incarcerated in the wound, especially after vitreous prolapse.

In a certain number of cases epithelium grows in from the wound and closes the anterior chamber. In this way the outlets of the eye are blocked, and secondary increased tension takes place.

One of the most feared and rarer complications following cataract extraction is the so-called expulsive hemorrhage. This takes place from the choroid, and may occur from the time of operation up to two or three hours afterward. The patient complains of great pain. Blood is soon seen soaking through the bandage, and if the eye be opened, a blood clot containing much of the lining membrane of the eye may be seen protruding from the gaping lips of the wound. In practically all these cases, the sight is lost, and it is best to remove the eyeball as soon as possible. According to different statistics, this accident occurs in from 0.1 per cent. to 0.4 per cent. of cases. Expulsive hemorrhage is due to disease of the vessel walls. There are five cases in the literature in which both eyes were operated on at the same sitting, and expulsive hemorrhage occurred in both.

Delirium, occurring two to three days after operation, is not infrequently observed, and need not give rise to alarm. It seems to be due to the exclusion of light; therefore, it is best to remove the bandage from one eye.

Before the introduction of asepsis, the eye was lost in from six to ten per cent. of cases of cataract extraction from suppuration. Von Graefe's method of linear extraction reduced this figure down to from two to five per cent. of losses. With the modern methods of operating, the mortality has fallen to in the neighborhood of 0.5 per cent. In addition to suppuration, the eye may be lost from hemorrhage, from severe iridocyclitis, or from glaucoma.

Reclination or Couching.—Reclination or couching is the displacement of the lens from the visual axis to the lower part of the vitreous. This procedure is of great antiquity, and was the principal operation done by the ancients for cataract. In the middle ages the cataract prickers (Staarstecher), as they were known, went through Europe from fair to fair couching cataracts. Couching is still practised to a considerable extent in India.

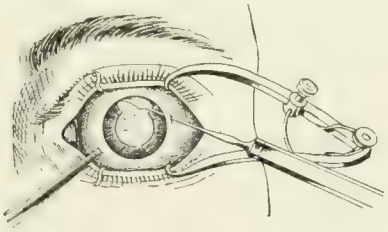

Fig. 1256.—Reclination (Scleronyxis Anterior) with Preliminary Iridectomy. (After Axenfeld from Wood's "System of Ophthalmic Operations," The Cleveland Press.)

Major Eliot declares that, according to his experience, forty per cent. of the eyes operated on by the natives are lost through sepsis, and it is not improbable that fifty per cent. of eyes upon which reclination is done are lost either through sepsis or through the development of chronic iridocyclitis and glaucoma. Various surgeons in modern times have recommended couching in certain cases, such as very old and feeble persons with bronchitis or asthma, also in hemophilia, where one eye has been lost from expulsive hemorrhage. It is also recommended for the insane.

The mode of operating was as follows: The cataract needle was passed through the sclera near the outer limbus and below the horizontal plane, passing in

front of the iris, to the surface of the lens. Or the sclera was penetrated back of the ciliary body through the posterior chamber to the anterior surface of the lens. Pressure was then made either to depress the lens into the vitreous, or to turn it over down into the vitreous; the first procedure, strictly speaking, being known as depression or couching, while the second was called reclination. As the lens disappeared from the pupillary space, the needle was held in position, pressing it down for a few moments, and then the point was wholly raised to see whether the lens would follow. If it rose up into position again, the operation was repeated.

Discission or Needling.—In youth lenticular opacities, either congenital or acquired, are soft cataracts, and are suitable for needling. The operation is permissible up to the age of twenty-five or thirty. The instruments needed are the speculum, the fixation forceps, and the knife-needle or a sickle-shaped needle. The patient should be recumbent. Although the pain is not excessive, the subjects are usually young, and consequently nervous. As it is important that sudden, spasmodic attempts to close the eye should not be made, anesthesia is often desirable. The pupil should be fully dilated with atropine. In some cases, it is impossible to see sufficiently well by daylight, and some form of artificial light with a condenser should be used.

The speculum is introduced, and the surgeon then grasps the globe with his fixation forceps. The point of entrance is variously chosen, but should be close to the limbus and through the conjunctiva. The blade is carried parallel to the plane of the iris, into the anterior chamber, and down to the lower periphery of the capsule. The handle of the needle is then raised, and the cutting edge turned toward the lens. An incision, some three or four millimeters long and one millimeter in depth, is made in the lens. The knife is then quickly withdrawn, and if it is properly designed to fill the wound completely no escape of aqueous will follow.

A bandage may or may not be used after operation, and is seldom of value after twenty-four hours. A shade covering both eyes should be worn, and the pupil must be kept permanently dilated with an atropine solution of suitable strength.

If there are marked symptoms of reaction, as indicated by watering of the eye, undue injection or local pain, strict quiet should be enjoined and hot fomentations applied. It is important to watch for increase in tension from excessive swelling of the lens, and if it ensues, paracentesis of the cornea must be performed without delay.

It is often desirable to regard the first operation as an exploratory one, to determine the amount of reaction which the eye is likely to show. If the swelling is not considerable, and absorption does not seem to be taking place at a satisfactory rate, a second needling may be done in four to eight weeks. In these cases, discission may be the only operation performed, and after it we may wait for a gradual absorption of the lens to take place. But in many cases, this is a waste of time, and the process may be greatly hastened by puncturing the anterior chamber and by evacuating the soft lens substance.

The great advantage of discission lies in its simplicity, and in the slight danger which so small a wound through the cornea entails.

The dangers of the needling operation are: glaucoma, iritis, iridocyclitis, and panophthalmitis. The occurrence of glaucoma has already been alluded to. If handled promptly, no harm can result. Non-inflammatory or chronic glaucoma may occur months or years after needling, through adhesions causing traction. If these adhesions be cut, the process usually comes to a standstill.

Iritis and iridocyclitis may occur from too rapid swelling of the lens substance. In a very small percentage of cases, severe infection and even panophthalmitis may occur. Von Graefe advised performing an iridectomy prior to discission. At the present day, this procedure is recognized as unnecessary.

Discission or dilaceration of membranous cataracts is not done to promote their absorption, for to a large degree they are composed of non-absorbable material, but rather to make a free opening in the membrane.

In former times the operation was much feared on account of the complications which occasionally occurred, iritis, iridocyclitis, suppuration and glaucoma; but since the adoption of asepsis, these dangers have been greatly reduced, until now it is well to operate in any case where a definite increase in vision is to be obtained.

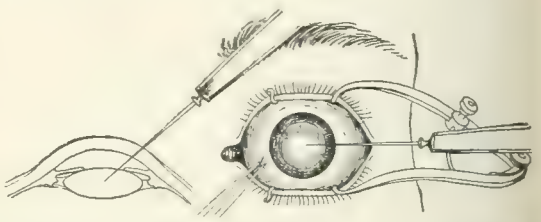

Fig. 1257.—Discission (Needling) through the Clear Cornea. The needle is directed forward to a point about one millimeter from the center of the dilated pupil, pushed about one millimeter into the lenticular substance and then a cut two millimeters long is made through the central area of the lens. (Wood's "System of Ophthalmic Operations," The Cleveland Press.)

As to the time of operation, it may be said that none should be performed until all signs of inflammation have left the eye. Some surgeons are accustomed to do a secondary operation two or three weeks after cataract extraction, while the very cautious ones may wait for three or four months.

For the operation itself, some form of artificial illumination should be used. The light may be focussed on the eye with a condensing lens, as it is very difficult to see just what is going on. In order to help the vision of the operator, Jackson advises the use of a binocular loupe. It is well to locate the center of the undilated pupil before operating for, owing to thicker adhesions on one side or to unequal elasticity, the opening made in the center of the dilated pupil may not be central after contraction takes place. It need not be said that the knife needle used for the operation must possess a point and blade of extreme sharpness, for often there is no more difficult task than to penetrate and saw through these membranes. In all operations upon the eyeball it is best, where possible, to make a wound that can be covered with conjunctiva, and this one is no exception to the rule. The knife should be introduced under the conjunctiva at the limbus before penetrating the anterior chamber. Much less difficulty is encountered during the operation if the shank of the knife completely fills the opening and prevents the escape of aqueous.

The operation most often performed is the single incision of the membrane. This incision sometimes fails, however, to produce an opening of sufficient size, or a good opening may be closed by a subsequent inflammation. The single incision operation does not differ greatly from the ordinary discission of a juvenile cataract.

The speculum having been introduced, the eye is grasped with fixation forceps and the knife needle is introduced, by ambidextrous operators, usually at the limbus slightly above or below the horizontal plane according to the location in the capsule previously decided upon. The anterior chamber is entered, the flat of the knife being held parallel to the plane of the iris, and is traversed until the knife is over the point

n the capsule where the incision is to be ma le. The utting edge is now turned toward the membrane, the handle is lifted, and the point plunged into the secondary cataract. With a sawing movement, an attempt is made to divide it on the blade. When the end of the incision has been reached, the handle is owered to its original position, the blade is turned and the instrument is quickly withdrawn, aiming to evacuate as little aqueous as possible.

Discission is sometimes performed with a very sharp thin cataract knife, but in using this it is extremely difficult during the manipulation not to enlarge the corneal incision and evacuate the aqueous. In the case of thick membranes which will not open sufficiently on being incised, it is often necessary to make more than one incision to allow the cut edges of the capsule to retract and curl back, leaving a sufficiently large opening. Such an incision may take the form of a V or a T, or a simple crucial opening may be made. To make more than one incision in a membrane of this description is often a difficult procedure, for the first cut is apt to relax the tension to such an extent that completion of a second incision is hard or even impossible.

Bowman devised a very useful operation for producing an opening in secondary cataracts. Two knife needles are introduced into the anterior chamber from opposite sides of the limbus, the eye being steadied by the first needle while the second is entered. Both needles are then plunged through a central point in the membrane, and by approximating the handles, the blades are forced apart usually tearing a large opening.

In the case of very thick secondary cataracts in which a satisfactory opening cannot be secured by any of the methods described above, it may be well to puncture the cornea and endeavor to remove the membrane by means of iris or capsule forceps. The result, though often a brilliant success, may be marred by iritis or iridocyclitis due to the trauma necessarily produced.

In those cases of after-cataract in which, owing to a plastic inflammation following extraction, there is a small pupil completely adherent, or in those where an iris prolapse has taken place and the pupil has been drawn up close to the corneal wound while the iris is stretched over the former pupillary area, it is frequently necessary to puncture the cornea, and by means of special scissors (de Wecker's) to remove a large enough area so that the pupil formed will not close.

Extraction of Cataract in Capsule.—In the olden times bordering on the birth of cataract extraction, attempts were made to extract the lens in capsule—first, it is believed, by Daviel and later by Sharp, Richter, Beer, Arnemann, and others. In the following years allusions are made to such an operation in the literature, but little progress was made until the question was taken up by Alexander Pagenstecher and by his brother Hermann. They argued that extraction in capsule removed all predisposition to iritis, that secondary operations were rendered unnecessary, and that better sight was secured by this than by any other method.

Beginning with a corneal incision downward, they later adopted the upward incision and conjunctival flap. A deep iridectomy was made to prevent iris prolapse, and with a dull hook posterior adhesions, if any existed, were freed. Pressure was then applied with a spoon over the upper scleral wound and counterpressure was made on the cornea, the eye being rotated downward with forceps. In case extraction by these methods failed, a flat spoon was passed down behind the lens, counterpressure made on the cornea and the cataract delivered.

This operation, although practised and modified by a number of ophthalmologists, never met with general approval, and extraction in capsule did not awaken general interest in the ophthalmological world until several East Indian surgeons began to perform it as a routine procedure.

As these so-called East Indian methods have excited in the English-speaking world of to-day some of the warmest ophthalmological discussions of the present time, it may be well to devote a little space to them.

The most prominent exponent of these methods is Colonel Henry Smith of Amritsar, formerly stationed at Jullundur. In 1895 Smith, seeing the good results of the extraction in capsule performed by Lieutenant Colonel Mulrowney, then stationed at Amritsar not far from Jullundur, decided to adopt similar methods as a routine and set about improving the procedure. Since that time, he has performed a vast series of extractions, and surgeons from many distant parts have visited his clinic to learn his methods of operating.

The important features of Smith's operation are as follows: The incision is made upward, and includes half or nearly half of the cornea. It is made with one stroke of the knife if possible, and is finished in the cornea. An iridectomy may or may not be made, according to the preference of the operator. The speculum is then removed and the upper lid controlled by an assistant, who holds it with a large strabismus hook, at the same time making pressure with his fingers on the orbicularis. The operator applies the rounded tip of a strabismus hook over the lower third of the cornea, and pressure is made in the direction of the optic nerve. The pressure is steady and the position of the hook should not be changed until the upper edge of the lens tilts forward and is seen to be dislocated. The pressure is then turned more and more toward the wound. The hook then follows the lens upward until the cornea is folded beneath it, the pressure gradually becoming lighter; at this point the lens is delivered.

In cases of immature cataracts and Morgagnian cataracts where the capsule is very delicate, he proceeds in a little different way finding that by the above method the capsule often bursts in the wound with the retention of capsule and other matter. In these he makes deep pressure over the lower border of the lens toward the patient's feet. The lens becomes dislocated below and turns up into the wound, making a complete half somersault. As the lens turns up into the wound, the operator directs his pressure first backward, then backward and upward, folding the cornea beneath the wound and delivering the lens by motions similar to those of the first method. The hollow of the strabismus hook may now be passed between the lens and the wound to complete the detachment.

In hypermature cataract hard of delivery, a spatula is dropped down behind the lens the instant it appears at the wound, and the lens is pressed against it with the hook on the outside of the cornea and made to slide out along the spatula, thus avoiding pressure which might produce a loss of vitreous. Careful reposition of the iris is of the utmost importance. If vitreous escapes, it is snipped off. No atropine is used. The eye is dressed and not disturbed until the eighth day.

The Indian statistics of this operation are extraordinarily good, and it has excited much interest, especially in America. Its great advantage is total extraction of the lens; its disadvantages, the additional danger of vitreous prolapse and the greater trauma. Its future place in ophthalmology is not decided. In the hands of an operator of the skill and experience of Colonel Smith, it is probably a very valuable procedure. In the hands of the inexperienced, it should be barred. Whether it will form a welcome addition to the surgical procedures of the man working under ordinary conditions of ophthalmological practice is still *sub judice.*

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Catarrh.—See *Mucous Membrane, Inflammation of.*

Catarrh, Nasal.—See *Rhinitis.*

Catatonia.—Under the name of catatonia, or katatonia (from κατά, down and τόνος, tension), or "tension insanity," Kahlbaum in 1874 described a composite form of mental disease, in which, with successive conditions of depression, excitement, and stupor, or one or more of them, there was muscular rigidity of cataleptoid character, peculiar mannerisms, and stereotyped movements with great resistivity, the whole process tending to end in more or less complete mental failure. In his view, this group of symptoms was limited to no special age. While the subject was long neglected and opinions regarding it have varied, through the influence of Kraepelin, these symptoms have assumed an important position and have come to be pretty generally regarded as characterizing one of the varieties of dementia præcox (*q.v.*).

Kraepelin defines catatonia as, "a disease form with a peculiar condition of stupor and excitement, usually ending in dementia and with the symptoms of negativism, impulsivity and eccentricity, stereotypy and suggestibility, in expressive movements and acts." While undoubtedly most common and characteristic in dementia præcox, the symptoms enumerated have been observed in paralytic, senile, traumatic, organic, and epileptic dementias, in constitutional defective conditions, and in melancholia. While in strictness, the term catatonia should be reserved for the symptom-complex, it has come to be applied quite generally to one of the forms of dementia præcox which is customarily described under this name. The etiology and pathology of catatonia are those of dementia præcox in general, and will be discussed under that head. The disease begins, as a rule, after a varying period of psychical depression, with vague hypochondriacal complaints. This may, however, attract little attention, the serious nature of the case being first made evident by some sudden violent or foolish act.

The preliminary period may be followed by an attack of excitement with hallucinations and illusions, of anxious, hypochondriacal character, or with phantastic religious ideas, during which the patient shows a tendency, by sudden and violent acts to injure himself or others.

The characteristic phases of the disease are those of stupor and excitement, which may succeed one another, often with great suddenness. Catatonic stupor presents most clearly the combination of symptoms which have given a name to the disease. The patient stands, sits, or lies in a stiff attitude. Any attempt at moving him is met with tonic resistance of the muscles, which sometimes show the peculiar rigidity of catalepsy (*q.v.*). The facial muscles are set in strained attitude, the forehead may be wrinkled, the lips pushed forward in a snout-like manner, and sardonic smile may occasionally draw up the angles of the mouth. Food is refused, saliva is allowed to collect in the mouth until it overflows, urine and feces are retained for long periods, to be discharged in the bed or in some other unsuitable place. Pin pricks in sensitive parts call forth no movements of defense, at most some reddening, or change in facial expression. The term stupor is a relative one, however, consciousness being little disturbed and the above train of phenomena—"negativism"—being due rather to inhibition. In apparent contradiction to negativism is the tendency to involuntary repetition by the patient of movements executed before him or suddenly ordered in a loud voice ("command-automatism"), or of words spoken by the examiner ("echolalia"). The stupor passing over into catatonic excitement, to mutism, negativism and refusal of food, there is added a peculiar motor impulsion. Monotonous movements are repeated over and over again, sometimes for hours at a time. The patient rhythmically turns or swings his body, claps or rubs his hands together, twists moustache or hair-braid, makes a certain number of steps forward and back, etc., etc. ("stereotypy"), all in a stiff and characteristic manner, the whole perhaps accompanied by a peculiar crying or screaming. He repeats over and over a monotonous phrase or a jumble of senseless syllables ("verbigeration"). Again he is impulsive and suddenly violent, smashes glass or furniture, assaults his fellow patients or attendants, masturbates, smears himself with urine and feces, makes sudden suicidal attempts, etc. Stupor and excitement may alternate with periods of comparative quiet, but throughout the whole runs the strain of the contrary, the stereotyped and the absurd. The keynote is negativism, with stereotypy of movement and of manner. The patient resists all attempts to bathe or dress him, refuses food set before him, only to seize suddenly and swallow greedily the portion of his neighbor. When taken to the closet, he retains urine and feces, to deposit them immediately afterward on the floor or in his bed. He is obstinately mute, or replies to a question by a sudden and abusive epithet, perhaps after some time. He gives unsuitable or perverted answers, talks baby-fashion, or with an affected or foreign accent, constructs new words, or jumbles together apparently unrelated words (the "word salad" of Forel). Apart from the periods of hallucinatory and emotional disturbance, sense of time and place is often well preserved, the patient being able some time later to tell correctly just what happened at a given time. The confusion is more apparent than real, being due to the negativism, which leads to silly and false replies. The patient will often acknowledge later that he has been acting perversely, in a foolish or childish manner, but explains that he could not help it. Attempts to analyze psychologically and to explain the phenomena of the characteristic negativism have been numerous of recent years, but beyond bringing out the facts that the behavior and the utterances of these patients are due not to mere foolishness, but rather to a struggle between opposing tendencies in the mental processes, the coordination of which, especially as between the intellectual and the affective attributes, having undergone a sort of fission ("schizophrenia"), they have done little to clarify the subject. In common with the other forms of dementia præcox, there is in catatonia, a dulling of the emotional and ethical feelings and a liability to senseless delusions, while ability to receive impressions, to comprehend, and to remember, is long preserved. Throughout, however, runs the tendency to mental failure, which proceeding steadily or with intermissions, may lead at length to an extreme degree of dementia.

As somatic symptoms in catatonia, besides the muscular phenomena already described, there have been noted a greater or lesser degree of analgesia, which in part explains the tendency to self-mutilation encountered in this disease, increased tendon reflexes, mechanical irritability of the nerve trunks, especially of the facial, muscular unrest, anomalies of glandular secretion, disturbance of the menstrual function, subnormal temperature, and trophic disorders, especially sudden and uncontrollable loss of weight, a fatal issue sometimes being due to inability to nourish the patient. Certain changes in the pupils, especially a failure to respond to psychical or physical excitement, as in normal people, has been observed, while Clark and Tyson have described certain changes in the eye

grounds. Epileptiform attacks are among the rare symptoms. Catatonia is preeminently a disease of the second and third decennia, but may occur later. While its tendency is always toward dementia, it often moves by successive steps, there being long intermissions, which may pass for recoveries. It is considered by Kraepelin as offering the most favorable prognosis of any of the forms of dementia præcox, but cure is in the majority of instances a recovery with defect, the patient having descended to a lower grade of mentality than he possessed before the attack.

In diagnosing our cases, it is to be remembered that the catatonic symptom-complex has been observed in a number of mental diseases. Depression with catatonia usually belongs to the præcox group. In cases of general paresis, in which the somatic signs are not characteristic, the results of the chemical and microscopical examination of the cerebrospinal fluid and of the Wassermann test applied to it and to the blood should tell the tale. In epilepsy the different history and the frequent convulsive attacks should settle the diagnosis, for convulsions are rare in catatonia. Hysterical insanity and catatonia present many points of resemblance and diagnosis between the two may readily be difficult and for a time impossible. A careful study will, however, detect points of difference, and clear signs of mental failure will stamp the case as one of catatonia. Imbeciles at times present the catatonic symptom-complex and when it is remembered that an originally defective person may in addition develop a dementing psychosis, the difficulties of diagnosis are evident. A careful study of the previous history of the patient should, however, give us aid in forming a correct opinion. Hallucinatory confusional conditions may at times resemble catatonia, but in them the clouding of consciousness and disorientation are usually obvious, and the motor phenomena are seldom so marked as in catatonia.

There is no specific treatment for catatonia, the various surgical measures addressed to the genital and the thyroid glands and opotherapy having proved unsuccessful. The best that we can do is to guard and nourish the patient and treat such symptoms as may arise. The majority of cases will require asylum treatment sooner or later.

Charles Lewis Allen.

Catechu.—*Cutch: Black Catechu.* An extract prepared from the wood of *Acacia Catechu* (L.f.) Willd. (fam. *Leguminosæ*). Catechu is similarly obtained from the wood of *A. suma* Kurz. That of the present edition of the British Pharmacopœia is discussed under *Gambir*. This species of acacia is a crooked, straggling tree of thirty to forty feet in height, with a trunk about a foot in diameter. It grows commonly in India and Burmah, and yields a very durable, hard timber and a tan bark. The sap wood is whitish, the heart wood of a very dark brown. It is said that both are extracted for the catechu, the process being by boiling the chips. The decoction, more or less purified by straining, is evaporated by artificial heat and is then moulded into various forms. The moulds are commonly lined with leaves, the remains of which adhere to the outer surface of the dried masses. The latter are of various forms and sizes, according to the custom of the locality or the convenience of the maker. The best usually come in the form of slabs or blocks, of the size and form of an ordinary bread pan. In India a superior quality, of a light brown color, is prepared chiefly for mastication by introducing sticks into the thickened decoction, when the catechu collects upon them, after the form of crystals. Dymock and Hooper ("Pharmacographia Indica," i., 558) describe a very high-priced sort which is collected from cavities in the trunk. This is called *Khersal* or *Khairsal*, and is of a very pale brown or yellow color. The description of catechu is as follows:

In irregular masses, containing fragments of leaves, dark brown, brittle, somewhat porous and glossy, when freshly broken. It is nearly inodorous and has a strongly astringent and sweetish taste.

If twenty parts of catechu be digested with two hundred parts of alcohol and the liquid filtered, the undissolved matter, after being dried at 100° C. (212° F.), should not exceed three parts in weight.

The tincture, diluted with one hundred parts of water, acquires a green color on the addition of ferric chloride T. S.

If two parts of catechu be boiled with twenty parts of water, a brownish-red, turbid liquid will be obtained which turns blue litmus paper red.

Upon incineration, catechu should not leave more than six per cent. of ash.

To this description it may be added that the color of some which is very good may be better characterized as a brown-black, and that a microscopical examination reveals the presence of a large quantity of minute crystals of catechin. Emphasis should be laid upon the fact that good catechu is nearly odorless. Much of what comes to our market possesses a vile odor. It is toughish, scarcely porous, and has a waxy or greasy looking surface instead of the lively, slightly sparkling luster of that which is pure. Such is largely used for tanning and similar purposes, but is not fit for medicinal use.

About one-third of catechu consists of *catechin* ($C_{21}H_{20}O_9+5H_2O$), and about one-half of *catechu-tannic acid* ($C_{21}H_{18}O_8$). The latter can be obtained from catechin by heating, especially with the addition of water or alkalies.

Catechu, as its composition would indicate, is a pure astringent, which may be generally used either externally or internally, when this effect is desired. We have official a compound tincture, of ten-per-cent. strength, with diluted alcohol and one-half per cent. of cassia, the dose fl. ʒ ss. to ij. (2.0–8.0). The official troches contain each six centigrams (about gr. i.) of catechu, with tragacanth and sugar.

Henry H. Rusby.

Caterpillars, Poisonous.—The caterpillars of several moths have hairs or spines on the back which secrete an urticating fluid. If they are touched, the hairs penetrate the skin and cause a severe prickling sensation. Ammonia may be used to relieve the irritation. Many caterpillars that are commonly supposed to be poisonous are, however, perfectly harmless. See *Insects, poisonous.* A. S. P.

Catgut.—See *Dressings, Surgical.*

Cathartics.—These (the term being derived from *καθαρτικός*, cleanser, especially in the present medical sense) are agents that promote evacuation of the bowels. Clinically they are divided as follows:

1. Laxatives which facilitate evacuation of the bowels but do not necessarily cause a passage as a direct consequence of their administration.

2. Purgatives, used to produce an occasional, single clearing out of retained feces.

3. Hydragogues (*ὑδραγωγός*, water-driver) are mostly salines and while used in small repeated doses as laxatives and in moderate dose as purgatives, are especially employed to eliminate dropsical effusions or the ordinary products of catabolism in cases of renal failure, or as part of a derivative effect upon the general distribution of blood and bodily fluids generally.

4. Cholagogues (*χολαγωγός*, bile-driver) were formerly supposed actually to stimulate the formation and elimination of bile. While such direct action has been disproved, their indirect action is such as practically to warrant the retention of the term as a matter of convenience.

5. Drastics (*δραστικός*, in the modern sense, but ety-

mologically referring to a running) act energetically, producing numerous evacuations, more or less congestion, and ultimately, in toxic dose, actual enteritis or gastroenteritis.

As regards their physiological actions, cathartics may be classified as follows:

1. Acting on peristalsis (*a*) by increasing peristalsis either directly or through innervation; (*b*) by correcting antiperistalsis which occurs normally in the colon and, as a reflex, from peritonitis and pressure upon or occlusion of the bowel; (*c*) by removing an inhibition of peristalsis.

2. Acting on intestinal contents (*a*) by softening a fecal impaction; (*b*) by supplying a sufficiency of gaseous contents or removing an excess leading to distention and paresis; (*c*) by increasing the watery contents; (*d*) by supplying a sufficient quantity of semisolid contents to afford a grasp for the peristaltic wave.

No sharp line can be drawn between the different groups of cathartics, according to the clinical classification, most vegetable cathartics being classed as laxatives, purgatives, or drastics, according to the degree of their activity which, of course, also depends upon dosage, although, even by modifying the dose, the same drug could scarcely be used as a member of the extreme groups. Certain of these have, in the clinical sense, a cholagogue action. Most of the hydragogues may also be used, according to dose, as laxatives, purgatives, or in the literal sense and in that of intensity of action, as drastics, though scarcely to the extent of producing an enteritis.

The theoretic classification as to method of action, should also be qualified by the statement that most cathartics act in more than one way. Illustrations of these methods, and the uncertainty of exact methods of action in many instances, will be noted later while the details will be considered under the names of each drug as they occur alphabetically and not in this article except as is necessary to give a comprehensive idea of the subject.

With regard to methods of administration, cathartics are ordinarily swallowed in solution, pill, tablet, capsule, etc. To prevent vomiting due to nauseous taste or to the inexplicable fact that many substances, even including foods, may be vomited when swallowed and retained if artificially deposited in the stomach, they are sometimes given by gastric or even duodenal intubation. This method is especially required in the management of insane, neurotic, and refractory patients. For the most part experimentally, administration may be by fistula or by direct injection through the coats of the bowel. Cathartic drugs may also be used by suppository (*q.v.*) or by enema (*q.v.*) or may be introduced fairly high in the bowel by a stiff tube (the ordinary soft "colon" tube never succeeding) or through a speculum. More recently, certain cathartics have been given subcutaneously or even intravenously and the cathartic effect of mercury and possibly other substances may be apparent after inunction or cataphoresis, though not designedly employed in this way. Nurslings are sometimes medicated by administering the drug to the mother.

1. Laxatives.—*Dietetic Measures.*—Many persons are constipated simply from lack of water to carry on eliminative action. When we reflect that the urine, respiratory vapor, and insensible perspiration amount approximately to a quart a day each, it is obvious that, with allowance for the 200 or 300 c.c. of water formed from carbohydrates, and the average of about 500 c.c. of water contained in ordinary solid foods of average consistence, rather more than two quarts of water a day must be taken either as such, in other beverages and soups, or in distinctly watery fruits and vegetables. As the ordinary beverages, coffee and especially tea, contain tannin, it is plain that the relief of constipation may rest solely on the substitution of water for these. It is scarcely necessary to state that water acts according to 2 *a* and 2 *c* of the above table, also facilitating the discharge of gases under 2 *b* and, up to a certain point, under 2 *d*.

Any food rich in indigestible residue is laxative by affording a grasp for intestinal peristalsis (2 *d*), by mechanically stimulating muscular action of the bowel (1 *a*) while, if regularly used, it prevents the formation of dense scybala (2 *a*). Such foods also tend to have a laxative effect by affording a pabulum for bacteria. Large dense masses, as bits of bone, fruit pits, etc., should, of course, be avoided, though they are not as dangerous as might be expected; and indigestible but putrescible animal tissues, as cartilage, connective tissue, and skin, should also be avoided. Vegetable cellulose is largely but variably decomposed into methane and other gases (2 *b*) but this action should not be allowed to become excessive. Small seeds sometimes produce irritative diarrhea, sometimes become impacted and may remain weeks or months in the bowel. Scales and chaff are also liable to adhere to the wall of the alimentary canal and, if sharp, may produce minute ulcerations. The danger of actual perforation or of entry into the appendix is slight but real. Hence, cellulose administered as a dietetic laxative, should be confined to spongy masses as in fruits, leaves, bulbs, heads, stalks, corms, tubers, and roots of more or less nutritious food stuffs, and to soft bran or whole wheat, well ground, although fine sawdust and pipe clay have also been used for the purpose of affording a soft, massive intestinal content. Care should be used not to choose vegetables possessed of distinctly astringent qualities.

An excess of sugar, in almost any form, is strictly hydragogue by osmosis (2 *c*). Digestible fats and oils act somewhat as lubricants and to soften scybala, like mineral oil, but, being converted into glycerin and fatty acids which unite with alkaline bases to form soaps, they tend to stimulate peristalsis (1 *a*). Glycerin alone may also be administered. It is probably not nutritive directly but, being hygroscopic acts as a hydragogue (2 *c*) and seems to stimulate peristalsis directly (1 *a*) being especially used as a rectal injection or incorporated with gelatin into a suppository. Moreover, an excess of any nutritive principle, starch or sugar, fat or oil, protein, favors saprophytic action with the production of various substances more or less irritating (1 *a*). Proteins and especially the purin compounds associated with animal proteins are toxic though probably not so much so as the partly metabolized products from an excess of fat. The fermentation of carbohydrates yields mainly carbon dioxide and water (2 *b* and 2 *c*) which are scarcely toxic. Whatever foods are used in excess as laxatives usually add a considerable amount of indigestible material (2 *d*). While in the absence of mechanical obstruction and marked depression of peristalsis, dietetic measures usually suffice to overcome constipation, it is a good rule never to employ them to excess, that is beyond the point at which saprophytic action becomes noticeable. It is far better to use drugs or even to leave the patient in a constipated state.

Laxative Drugs.—Pure mineral oil (purpetrol), being neither absorbed nor decomposed, acts as an intestinal lubricant and hence renders peristalsis more effective, it disintegrates scybala (2 *a*) and, by coating over local lesions prevents reflex inhibition of peristalsis (2 *c*). It is especially indicated in infants, whose anatomy is such that peristalsis always acts against relatively acute angles in the colon and sigmoid, and as a palliative in incomplete strictures. Animal gelatin seems to favor easy movement of the bowel in somewhat the same way while vegetable gelatins, as agar-agar, which swell by inbibition of water but do not dissolve, afford a bulk of easily propelled contents (2 *d*).

Among laxative drugs may be mentioned sulphur, phenolphthalein, rhamnus purshiana, compound licorice powder, tamarind, manna, euonymus, etc. Small doses of those classed as purgatives may also be used, including the milder salines, especially sodium phosphate, but the prolonged use of salines is apt to diminish the secretion of hydrochloric acid and thus not only to interfere with gastric digestion but to lessen the amount of effervescence produced by the action of chyme on the carbonates of the biliary, pancreatic, and intrinsic intestinal secretion, the carbon dioxide thus formed being of considerable importance in the normal stimulation of peristalsis (2 *b*). Again, sodium and potassium salts, used in small dose with the idea of producing a laxative effect, are very likely to act rather as diuretics. Another practical point is that the salines are mainly hydragogue and, if needed only for a mild laxative effect, the real indication is usually for a more abundant supply of water. The vegetable laxatives act principally by stimulating peristalsis (1 *a*). The method of action of sulphur is not well understood but it exerts a mild stimulant action on mucous membranes and supplies an ingredient for taurocholic acid which, itself, stimulates peristalsis. Phenolphthalein is generally regarded as a stimulant of peristalsis (1 *a*) though it is asserted by some that it is hydragogue (2 *c*) and that it is not absorbed. The last statement is incorrect as the urine can be titrated, using the eliminated phenolphthalein as an indicator, provided, of course, that a sufficient dose has been given, say five to ten centigrams a day.

2. Purgatives.—The more closely the underlying causes of constipation are studied, the more rarely does one encounter the simple indication of securing a single clearing out of the fecal mass—purgation. Still, this indication exists practically as a preliminary to the more careful study of many cases, even to facilitate palpation or examination by speculum; also as a routine initial treatment of most cases in which foul, fermenting feces are present, and at the beginning of most fevers, including colds; also merely because the patient seeks only temporary aid. Perhaps the best purgative is castor oil, especially for children, and most surgeons believe that it acts better than any other to sweep out scybala and adherent masses from nooks in the intestine, as a preliminary to operation. It acts both as an oil and through the stimulation of both peristalsis and secretion by its active principle (1 *a* and 2 *c*). It is said to leave a state of constipation behind but this is probably tantamount to saying that its action is temporary and that, having thoroughly evacuated the intestine, a period of quiescence naturally results pending the accumulation of feces.

Seidlitz powder supplies artificially the carbon dioxide normally formed by interaction of acid chyme and carbonate-containing secretions and also acts as a hydragogue (2 *c*). Effervescent magnesium citrate and other effervescent salines have a similar action. Recent experiments however tend to emphasize, especially for magnesium, a direct peristaltic stimulation (1 *a*). It is commonly held that such drugs are not efficient unless the system is abundantly supplied with water and unless the patient is more or less active. These limitations are not absolute, however.

Magnesium oxide and hydroxide are especially employed to combat hyperchlorhydria, their concomitant laxative or purgative effect being sometimes desired and sometimes not. Magnesium sulphate is more active than other preparations, perhaps solely on account of is bitterness, as in the case of vegetable cathartics. It sometimes nauseates and produces considerable griping but an absolutely pure preparation is comparatively lacking in these objectionable features.

Sodium sulphate, potassium and sodium tartrate, potassium tartrate, sodium phosphate, etc., are also employed, acting like magnesium salts but not quite so powerfully, perhaps because thay are purer hydragogues. Sodium phosphate is commonly regarded as having an especial cholagogue action.

3. Hydragogues.—These include the various salines, already discussed and, with them are usually included jalap and elaterium and sometimes others of the drastic group, *q.v.* There has been considerable dispute as to the reality and exact nature of a hydragogue action. The inconsistencies of early experiments have, however, been harmonized to a large degree by attention to the general principles of osmosis and molecular tension. It is now generally conceded that any saline given in concentrated solution, of higher tension than the blood plasma, will call forth a secretion into the intestine. This is not a mere transudate, lacking albumin and globulin, nor a mere filtration since it contains active ferments. It has, however, also been shown that magnesium and other metallic salts are absorbed from the small intestine, and to some degree eliminated through the kidneys. On the other hand, even when directly introduced into the circulation, they are eliminated largely by the intestine and have a cathartic action which can scarcely be considered hydragogue, but depends upon direct stimulation of peristalsis. (See below.) While hydragogues are used as purgatives when there is a contraindication to other drugs, or by general choice, when there is no definite indication except to produce free evacuations, their special field is the elimination of water and toxins, either along with diuretic and sudorific methods, as in various forms of dropsy, when their efficiency, though not the actual amount of intestinal discharge immediately produced, is increased by a relatively water-free and salt-free diet, or vicariously in case of renal failure.

4. Cholagogues.—Animal experiments do not support the theory of a direct stimulation of the secretion of bile by drugs, except to a certain degree by salicylic acid and its congeners and by bile salts themselves. It is possible, however, that further experiment may show strictly cholagogue tendencies on the part of other drugs and may detect fallacies in regard to those apparently demonstrated not to be cholagogues. However, "biliousness" (*q.v.*) is now interpreted not so much as a failure of biliary secretion as of abnormal states of the biliary passages, toxemia from saprophytic action in the bowel, and disturbances of portal circulation. Thus, the cholagogues continue to fulfill the clinical indications, though on a different explanation and, for the sake of convenience, the name may be retained.

Calomel and other mercurial cathartics, although not notably diminishing the number of bacteria per unit of feces, in ordinary dose, limit saprophytosis both by removal of foul feces *en masse*, like any other cathartic, and, apparently, by diminishing bacterial virulence, so that indican is reduced in the urine and indol, its precursor, in the feces, the statement being made in an apparently illogical order because of the greater convenience, rapidity and delicacy of the urinary test. Calomel also prevents the reduction of bile pigment—the most toxic constituent of bile—and favors its removal, along with other biliary constituents and fecal masses generally. Ordinarily, the biliary salts are reabsorbed and reexcreted. It is obvious that, even without any direct cholagogue action, the elimination of biliary salts calls for renewed secretory action on the part of the liver, in accordance with the general regulative function of all organs of the body, although the nature of this regulation is not well understood. Being relieved of the toxic action both of biliary pigment and of bacterial products, the liver is better able to perform this function. Hence, ultimately, a real cholagogue action is produced, though this would not be apparent in comparatively brief experiments on lower animals normal save for artificial interfering factors. The advantages of ad-

ministering calomel or other mercurials in small divided doses, followed by castor oil or a saline need only be mentioned here. With the small dosage necessary, even the presence of hydrochloric acid rarely causes sufficient oxidation to the mercuric form to cause any danger.

In passing, may be mentioned the administration of 30 to 500 grams of metallic mercury to relieve volvulus, intussusception, and other mechanical forms of obstipation. This method is not one of catharsis but depends upon the weight of the liquid mercury, not enough entering into chemical combination to have any appreciable physiological action, unless long retained. While this method has fallen into disrepute, the accidents theoretically to be expected are not indicated by experience, and while it should not be allowed to excuse the delay of radical interference beyond a reasonable time, it seems to have much in its favor.

This is an appropriate place to make the general assertion that no cathartic should be pushed beyond a reasonable degree in the attempt to overcome an obstacle to evacuation of the bowels. Even mechanical efforts at dislodgment or disengagement, from below, should not be persisted in to the degree of weakening the strength of the patient and of postponing operative interference beyond the favorable stage. The significance of the phrase "obstruction of the bowels" should be clearly appreciated. Obstruction merely to fecal discharge, is not an emergent matter, complete obstipation may last for weeks or occasionally months without actual danger to life. The emergent "obstruction of the bowels" refers to obstruction, not of the lumen, but of the structure of the intestine, in other words of the vascular supply, rapidly leading to necrosis. It is necessary to qualify this statement with the corollary that obstruction of the lumen often causes or coexists with obstruction of the blood-vessels, and that trophic influences must also be considered.

5. Drastics.—A great many drugs, especially of vegetable origin, containing acrid resinous principles, cause more or less acute gastroenteritis, with vomiting and purging, when given in sufficient dose. Most such drugs are not employed in modern medicine as cathartics, some are valuable otherwise, some regarded merely as poisons. Those commonly classified as drastic cathartics, are, in ascending order of severity of action: jalap, scammony, colocynth, podophyllum, gamboge, elaterium, and croton oil While the dose is regulated so as to avoid any true inflammatory effect, more or less congestion of the abdominal and pelvic organs is produced so that, on the one hand, these drugs may be employed in functional amenorrhea and, on the other hand, should be avoided in pregnancy. The same is true in less degree even of senna, rhubarb, and aloes (in ascending series to the rather arbitrary line between purgatives and drastics). Podophyllum is reputed to have an especial cholagogue effect while jalap, colocynth, and elaterium are classed also as hydragogues, although rather by inducing a free secretion by irritation than by an osmotic process. The compound jalap powder, containing sixty-five per cent. of potassium bitartrate is naturally, more truly a hydragogue and, perhaps merely because inert samples of jalap are used, often a very mild and safe cathartic. The drastics are often given combined with one another and with calomel and other cathartics, also usually with aromatics, belladonna, etc., to relieve griping. It is not worth while to enter into a criticism of the compound cathartic pill. Croton oil, being the most energetic cathartic known for anything like comparable doses, is especially used for its derivative effect in cerebral hemorrhage but its actual efficacy is always doubtful. It is also used in suspected malingering, hysteria, etc., either to demonstrate the falsity of a claim of obstipation, or as a veiled punitive measure. The more closely conditions of constipation are analyzed, the greater is the tendency to avoid the drastics, or to reduce the dose of any cathartic so that the effect would not justify the use of this term. Any tendency to intestinal ulceration, inflammation, or even acute congestion, or the presence of tumor, even hemorrhoids, or other lesion liable to exacerbation by an increase of blood supply, is a contraindication. The contraindication with regard to a possible abortifacient effect has been noted. On account of the resinous principles of most of these drugs, any tendency to hemorrhagic or inflammatory conditions of the genitourinary organs, also is a contraindication. Cardiac weakness and fibrosis or calcification of the vessels also contraindicate the use of drastics, unless perhaps in the event of existing hemorrhage when a derivative effect is desired.

Cathartic Adjuvants.—The use of enemata and suppositories, electricity, massage, exercise, etc., will be discussed under those headings.

Atropine or belladonna and hyoscyamine or hyoscyamus (hyoscine being too depressing and having too little effect upon the intestine to be used specifically in this connection) are frequently employed as adjuvants, especially to purgatives and drastics of vegetable origin. The primary effect of minute doses is rather constipating, apparently by jointly lessening secretion and stimulating inhibition of peristalsis. With larger doses, inhibition is itself inhibited and a freer secretion occurs. Ultimately, there is paralysis of peristalsis. The therapeutic effect is limited to the second stage unless, as in biliary or intestinal colic, the indication passes beyond that under discussion, to that of relaxation. In lead colic, reflex inhibition of peristalsis from anal fissures or other painful lesions of the outlet of the bowel, and remote causes of similar reflexes, local and general anodynes may be indicated, including atropine and hyoscyamine or substituting stronger drugs for these. In such cases, even opiates may have a cathartic action.

Strychnine promotes the response to excitomotor stimuli generally. Rarely, it causes a distinct looseness of the bowels. It is often combined with belladonna as a cathartic adjuvant, especially in the pill of aloin, strychnine, and belladonna.

Various volatile oils or aromatic crude drugs, including the ordinary spices, may be combined with cathartics to lessen griping. This effect is due in part to a local anesthetic action, in part to a reflex stimulation of secretion and antiseptic action, both of which tend to prevent irritation by undigested and decomposing contents.

X-ray Investigation of the Pharmacology of Cathartics.—Some allusion has already been made to experimental study of the action of cathartics. Unfortunately, the highly artificial and disturbing factors of vivisectional study, have resulted in rather conflicting views although these have, for the most part, been harmonized, and usually in such a way as to corroborate clinical experience. The x-rays have facilitated the study of peristalsis and thus simplified the problem of distinguishing between this and secretory action in drawing conclusions from physical and chemical studies.

Glassner and Singer[1] agree with previous conclusions that the peristaltic stimulant of bile consists in the biliary acids '(occurring as salts, mainly of sodium, in the bile). They have shown that this action is almost entirely confined to the large intestine whereas, normally, the biliary salts are reabsorbed for the most part before the large intestine is reached. Hence they advise the injection of bile or its salts or of cholic acid into the rectum, or the use of ten to twenty centigrams of cholic acid in suppository. Almost any preparation of bile, as an extemporaneous watery mixture of inspissated bile, acts well when thrown high into the rectum or into the sigmoid, as through a

rather stiff and large rectal tube or the sigmoidoscope, but there seems to be no question that a reasonable dose of inspissated bile, by mouth, reaches the large intestine in sufficient amount to stimulate peristalsis.

R. Magnus[2] confirmed by Stierlin[3] holds that senna also has no action on peristalsis till the colon is reached, when powerful direct peristaltic waves begin and continue till all of the drug has been expelled. Magnus ascribes to castor oil, an action on the muscle of the stomach and all of the intestine, though the oily consistency of the drug rather counteracts its essential effect while it remains in the stomach. However, as well known clinically, there may be considerable stimulation of gastric peristalsis, even leading to vomiting.

McCallum[4] supports the theory of Aubert, expressed several years earlier, that hydragogues, especially salines, act strictly as stimulants of peristalsis, after absorption from the upper intestine, or when directly introduced into the circulation. Hertz, Cook, and Schlesinger[5] find that it requires about four hours for bismuth to reach the cecum after leaving the pylorus. The coincident administration of magnesium sulphate does not shorten this period although purgation may occur before the bismuth reaches the cecum, on account of the stimulation of peristalsis in the lower bowel. While these various experiments do not contradict the hydragogue effect of concentrated solutions of salines up to the point at which the intestinal contents have reached an equilibrium with the blood plasma, it is noteworthy that the watery passages precede the elimination of the bulk of the salt from the bowel. This latter occurs in the relatively solid stools of the day following the liquid purgation.

Hypodermic Purgation.—The therapeutic possibilities indicated above have been verified clinically by Robin and Sourdel[6]. One-half to 1, or at most 5 c.c. of a twenty-five-per-cent. solution of magnesium sulphate, injected subcutaneously with aseptic precautions, act effectively, obviously in this way as a peristaltic stimulant and not as a direct hydragogue according to the osmotic theory. Barnet[7] employs 2 to 20 c.c. of a one-per-cent. solution or 1 to 30 c.c. of a ten-per-cent. solution of magnesium sulphate. He also corroborates Zulzer and Dorn's advocacy of peristaltic hormone, especially as a hypodermatic remedy; and has used sterile infusion of senna, 1 c.c. of a five-per-cent. solution, or *vice versa;* solution of extract of rhamnus purshiana and of phenolphthalein, the latter with a small addition of sodium carbonate. Credé[8] employs a concentrated, active principle extract of senna, called sennatin, in a dose of one to three grams. Emodin and chrysophanic acid soon appear in the urine, which becomes darker and of a reddish color.

The indications for subcutaneous purgation are: (1) Anything preventing the use of the mouth, as incessant vomiting; lead colic; voluntary poisoning and resistance to medication (when both apomorphine and purgatives may be administered subcutaneously); coma, etc. (2) Requirement of too small a dose to be efficient by mouth, or contraindication to local irritation, as in gastric or other ulcer, inflammation of the appendix, gastroenteric spasm, etc. (3) Need of continuous action, as when the digestive tract has been exhausted by laxatives or by anesthesia.

A. L. Benedict.

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4. Am. Journal of Physiology, 1903, p. 101; 1909, p. 259.
5. Proceedings of the Royal Medical Society, 1908.
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Catheterism of the Ureters.—See *Urinary Segregation.*

Catheterism, Urethral.—Three important factors are to be remembered in introducing catheters into the urethra, namely, cleanliness, gentleness, and lubrication. In every instance the catheter should be sterilized by heat or chemicals; the hands of the surgeon should be well scrubbed; and the penis (or vulva) well washed and surrounded with sterile towels. The patient reclines with the shoulders somewhat elevated and the knees slightly flexed. All instrumentation is contraindicated when acute urethritis exists. The kind of catheter to be selected depends upon the

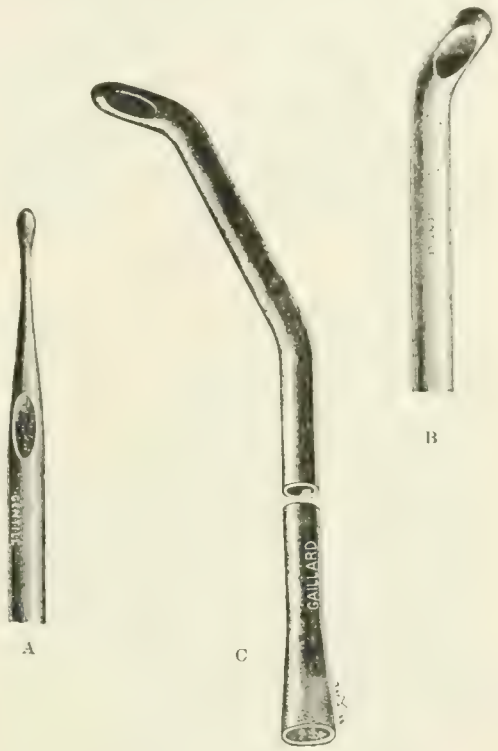

Fig. 1258.—Catheters. *A*, olivary tip; *B*, coudé catheter; *C*, double coudé catheter.

character of the obstruction which demands the catheterization. Generally speaking, medium sized soft-rubber catheters are to be preferred unless a tight stricture of the urethra or hypertrophy of the prostate is present. In case the latter exists the woven coudé (elbowed) or bicoudé (with two bends) catheters should be used as the end of the catheter is thereby carried along the roof of the urethra which is always less abnormal than the floor. The shaft of the catheter should not be touched by the operator unless his hands are covered with sterile rubber gloves. In order to avoid this when using soft-rubber catheters a metal stilet should be introduced about three-fourths the length of the catheter so that it will not bend when held near the outer end. The woven catheters have the advantage of being stiffer than the soft-rubber ones.

Most of the improved catheters can be boiled and thus sterilized, or they may be sterilized by formalin gas. When the latter method is used the catheter should be subjected to the formalin gas for not less than eight hours. If one does not possess a catheter-ostat, glass tubes may be secured at a nominal cost and with a cork in each end provide satisfactory apparatus. The catheter should always be well

cleansed before being placed in the glass tubes and if used on infected patients should be boiled. The catheter should then be wiped dry and dusted with talcum powder and placed in the tube. A bit of cotton is moistened with formalin and inserted just within the glass tube, and the cork is inserted so as to hold it in place. The formalin should not be allowed to reach the catheter or it may cause it to stick to the tube. Before being used the catheter should be immersed in a two per cent. solution of carbolic acid for a few minutes so as to dissolve the formalin and prevent urethral irritation.

Fig. 1259.—Silk Woven Prostatic Catheter.

No urethral instrument should be hurriedly introduced. If slowly and gently passed the muscles relax and little pain or traumatism is produced. If difficulty is experienced in inserting a medium sized soft-rubber catheter a smaller woven one with a bend at the end should be tried. If this fails to pass, others with two bends or other shapes may be used. Finally if all fail an endoscopic tube should be introduced

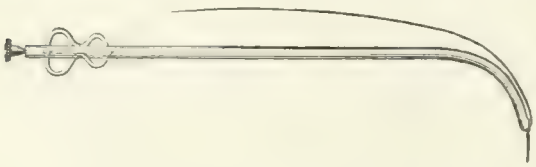

Fig. 1260.—Gouley's Tunneled Catheter Guide.

to the obstruction and whale-bone filiforms introduced one after another until the bladder is entered.

The filiform may be tied in place for twenty-four hours or it may be followed immediately by a tunneled metal catheter, into which the outer end of the filiform is threaded and thus guides the metal catheter along the urethral canal rather than allowing it to pass into pockets or false passages.

If the meatus is too small to permit the passage of the catheter, meatotomy should be done. In order to prevent the pain on urination and the necessity for subsequent instrumentation to keep the cut surfaces from growing together, the incised area should be cauterized with a saturated solution of nitrate of silver in concentrated carbolic acid. A tourniquet should be previously applied so as to stop the bleeding before the cauterization and care taken not to smear the solution in the urethra or on the penis. No dressing or after-treatment is required. Instrumentation may be done at once after meatotomy so performed.

Fig. 1261.—Filiform Bougies; Olivary, Angled, and Twisted.

One of most satisfactory lubricants is "medium" lubricating oil as used for motor cars; this is like liquid vaseline and takes in solution nitrate of silver or cocaine. The former may be dissolved two grains to the ounce or the latter in a saturated solution or the oil may be injected without medication. It should be sterilized in an autoclave in steam under pressure or by boiling in a porcelain vessel. After cleansing the meatus and penis two drams of the oil with or without medication should be injected with a sterile, blunt-

pointed urethral syringe. In this manner the urethra is lubricated and the catheter slides readily over the mucous surface causing little pain or traumatism.

In case residual urine is present to a considerable extent all of it should never be withdrawn at once as it may cause hemorrhage, shock, or anuria. If hematuria already exists and clots block the eye of

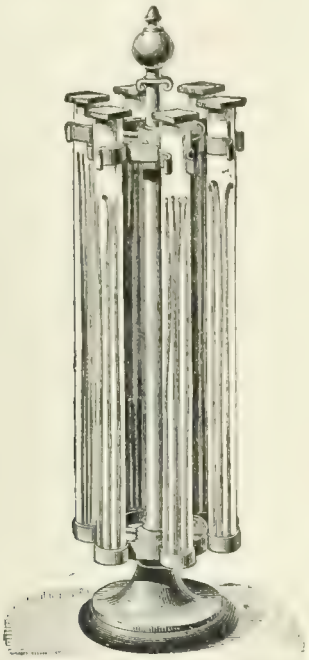

Fig. 1262.—Hermetically Sealed Glass Tubes for Storing Sterilized Catheters, with Convenient Form of Stand.

the catheter they should be drawn out by suction applied by a large piston syringe.

In catheter life of prostatics great care should be exercised to prevent as long as possible the infection which is almost certain to follow continued catheterization under such circumstances. The back pressure from the urine, however, will soon seriously damage the kidneys so that we are between two serious

Fig. 1263.—Catheterism; first stage.

dangers, *i.e.* infection and nephritis. Prostatectomy should therefore be performed before such damage has become extensive.

If one is unable to pass a catheter into the bladder through the urethra a trocar and cannula should be inserted about one-half inch above the symphysis pubis (the bladder being distended) and a catheter passed through the cannula into the bladder. The cannula is withdrawn leaving the catheter in place which should then be pulled out until it cannot pass into the neck of the bladder which would cause tenesmus. Drainage is in this way secured until more radical measures may be adopted. The cannula

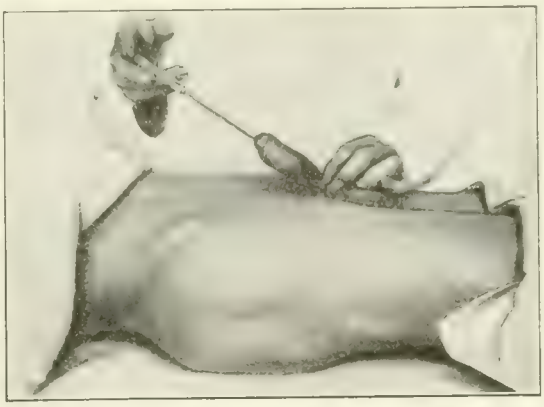

Fig. 1264.—Catheterism, second stage.

Fig. 1265.—Catheterism; third stage.

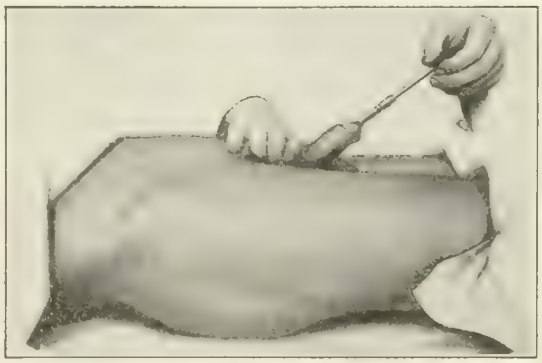

Fig. 1266.—Catheterism; fourth stage.

should admit a 12 F. soft-rubber catheter. The suprapubic region should be sterilized with tincture of iodine and the point for the insertion should be anesthetized with two per cent. alipin or novocain. Practically no pain or shock is caused by this procedure. The catheter is held in place with a silk

suture passed through the skin and catheter. Sterile gauze is placed around it and secured with adhesive plaster. A clamp is placed over the catheter and its outer end is kept surrounded with sterile cotton. If

Fig. 1267.—Catheterism: final stage.

necessary the catheter may be replaced at the end of a week by a fresh sterile one of somewhat larger size. The patient may void his urine when necessary through the catheter, and argyrol or other medication may be injected as desired. Edgar G. Ballenger.

Catnip.—*Cataria, Catmint.* The leaves and flowering tops of *Nepeta cataria* L. (fam. *Labiatæ*). This large and showy herb of Europe and Asia is very abundantly naturalized in the United States. It grows about deserted houses, barns, and in similar waste places. It becomes four or five feet high, and almost as broad, and, branching from the base, forms a pyramid of inflorescence, the flowers very small but very pretty. It is peculiarly aromatic and derives its name from the fondness of cats for it, which incites them to the most curious demonstrations. They not only eat it, but roll in it, and evince the utmost joy, and apparently affection, in its presence. Larger animals of the cat tribe, such as lions and tigers, act similarly, and great excitement may be caused at the "zoo" by introducing it into the cages. With a small amount of volatile oil and an amaroid, it is a very mild aromatic bitter. It is usually given in decoction, in large doses, the warm water aiding its diaphoretic action. Henry H. Rusby.

Catoosa Springs.—Catoosa County, Georgia.

Post-office.—Catoosa Springs. Hotel and cottages.

Access.—From Atlanta and Chattanooga via the Western and Atlantic Railroad. Distance north from Atlanta, 115 miles; east from Chattanooga, 26 miles; from railroad, 2 miles.

This resort is nestled among the mountains of North Georgia at an elevation of 945 feet above the sea level. The aspect of the country is quite rugged, the Sandstone Mountain, about a mile distant, reaching an altitude of 1,800 feet above the tide water. From the summit of this mountain may be seen Mission Ridge, the historic Lookout Mountain, and many other points of lesser interest. The hotel and cottages at the springs have room for several hundred guests, and are supplied with all modern conveniences. The climate is bracing and invigorating, even in the summer months; in winter it is temperate. The springs are fifty-two in number, situated within an area of two acres. It is not unusual to find quite different properties even among springs only a few feet apart. Most of them are quite strongly mineralized, ranging in mineral ingredients from about 84 to 110 grains to the United States gallon. Following are analyses of three of the springs by Prof. W. J. Land, of Atlanta:

One United States gallon contains:	Chalybeate Spring. Grains.	White Sulphur Spring. Grains.	Buffalo Spring. Grains.
Calcium sulphate	41.56	44.81	45.00
Magnesium sulphate	27.90	32.01	33.02
Strontium sulphate	.20	.21	.29
Sodium sulphate	1.59	1.67	1.67
Potassium sulphate	2.30	2.32	2.31
Aluminum sulphate	.67	2.47	2.39
Calcium carbonate	3.75	3.85	3.86
Magnesium carbonate	7.48	8.40	8.70
Iron carbonate	.19	.28	.28
Lithium carbonate	Trace.	Trace.	Trace.
Manganese carbonate	.01	.02	.12
Strontium carbonate	.04	.04	.04
Potassium carbonate	.11	.11	6.01
Sodium carbonate	.26	.26	.03
Calcium nitrate	.37	.32	.03
Ammonium nitrate	.11	.10	.91
Calcium bromide	.26	.15	.15
Magnesium bromide	.30	.31	.33
Calcium fluoride	.02	.02	.01
Sodium chloride	.14	.14	.11
Crenic and apocrenic acids	.02	.01	.01
Free sulphuric acid	.01	6.13	.13
Free carbonic acid	4.31	4.51	4.62
Hydrosulphuric acid		.02	Trace.
Total ingredients	91.60	108.16	110.02

All of these springs boil up through the hard black slate of the mountain side. They are perennial, the most severe and persistent droughts causing no perceptible difference in the rate of their flow. The waters are recommended for stomach, kidney, and bowel disorders, and for debility.

Emma E. Walker.

Cauda Equina.—Anatomy.—The spinal cord terminates as the conus medullaris, in the adult, at the second, in the young infant at the third lumbar vertebra. Hence, the lower spinal nerve roots, instead of passing directly outward, descend each until it reaches its proper point of exit, through the corresponding intervertebral foramen. The dura mater having been opened, this collection of nerve roots, viewed from behind, presents an appearance not unlike the hairs of a horse's tail (hence the Latin name). These nerve roots are regularly arranged, from the lowest, next to the median line, to the highest on the outside. The anterior and posterior roots are here separate, union not taking place until after they have pierced the dura.

Diseases.—The cauda equina is subject to injury, in fractures and crushes of the lower end of the vertebral column, from hemorrhages into the spinal canal, and may be involved in syphilitic and other forms of meningitis and in new growths in this region.

A *differential diagnosis* between affections of the roots alone and those involving the lower segments of the spinal cord is important, since, while in cord injuries there is little possibility of repair, the nerve roots have great capacity for regeneration if pressure upon them can be removed. A number of operations for the relief of such conditions have been performed with favorable results. Experience has shown that in moderate pressure upon the cauda equina, the inner roots suffer first, hence the symptoms are most frequently those of involvement of the sacral and coccygeal nerves. Paralysis may be caused by a pressure insufficient to produce anesthesia. Of course an injury may involve both nerve roots and conus medullaris.

Localizing diagnosis depends upon the anatomical and physiological considerations mentioned in con-

nection with spinal cord diagnosis (*q.v.*), for lesions of the nerve roots give symptoms similar to those of the corresponding segments of the spinal cord, with the exception that, while in nerve root lesion, the anesthesia and paralysis are of segmental distribution only, where the cross-section of the cord is involved, there are anesthesia and paralysis in the territory of all the segments below the injury. As the reflexes from the lower extremities all arise from the lower lumbar and sacral segments, by lesion of the roots of the cauda equina they can only be lessened

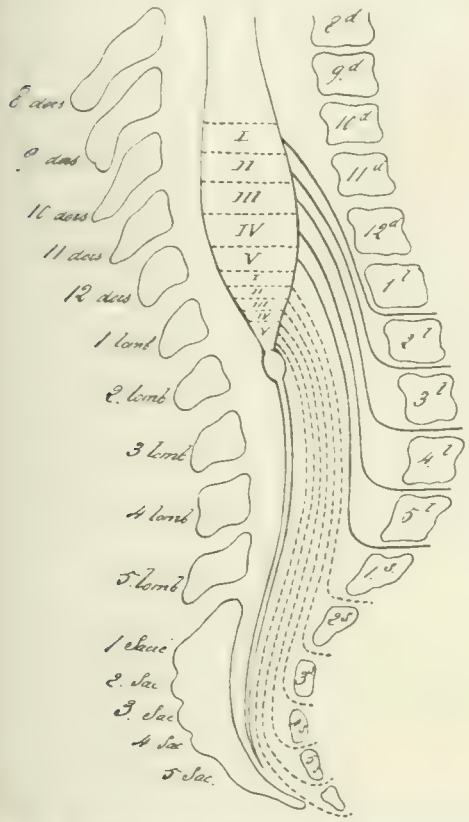

FIG. 1268.—Showing the Arrangement of Segments and Nerves of the Cauda Equina. (Dana.)

or abolished, never heightened. Hence any exaggeration of the knee-jerk or presence of the Babinski phenomenon would point to involvement of the spinal cord above the region of the conus. The location of an injury will give important diagnostic indications, since fracture anywhere below the second lumbar vertebra can cause crushing or compression of the nerve roots but does not involve the cord. A lesion of the lower half of the lumbar enlargement, and one of all the nerves of the cauda below the third lumbar will, however, produce practically identical symptoms. Since the inner nerves suffer most from pressure, and these are sacral and coccygeal, the usual symptoms of moderate compression of the cauda equina are anesthesia in a small saddle-shaped area over the buttocks and about the anus and posterior part of the genitals, with flaccid paralysis of the foot and peroneal muscles and loss of control of bladder and rectum. In lesions of the cauda, the symptoms are more apt to be unevenly distributed on the two sides than in those of the cord. When there is pressure upon the posterior roots there will be anesthesia if this is strong enough to put them out of function, otherwise irritative symptoms will prevail. Severe pain over the distribution of the sacral nerves is suggestive of a caudal lesion rather than a spinal one. Trophic disturbances, as bedsores, are much more frequent in spinal cord lesions than in those of the cauda. These latter do not produce dissociation of sensation, nor in them is the Brown-Séquard syndrome possible.

The *treatment* of diseases and injuries of the cauda equina does not differ from that of similar conditions affecting the spinal cord, except in so far as in the former, surgical intervention offers better prospects of success. CHAS. LEWIS ALLEN.

Caul.—This word, derived from the Gaelic *call*, a veil, is applied to the great omentum or any serous membrane, but its chief application is to the amnion, which at birth is sometimes delivered unbroken, enveloping the head of the child, or a piece of the membrane may be banded across the head or face, forming a scarf or veil, hence the name.

The caul is interesting on account of the superstitions which have surrounded and been associated with it from remote antiquity. Weston, in his "Moral Aphorisms from the Arabic" (1801), says that the superstition comes from the East, reference being made to it in Arabic literature. In every country where the superstition is found, a child born with a caul is the lucky possessor of good fortune of various kinds. As a caul was not always retained by the person born with it, it brought good fortune or protected from danger whoever possessed it. Each land has its own interpretation of the so-called luck.

Many stories are told of the faith of the early Romans in this sign. Roman lawyers, being no more confident of their abilities than the lawyers of to-day went to the market-place and secretly purchased the caul from midwives, who had, in all probability, pilfered the same from a child at birth. It was worn against the bare skin on the chest under the clothes, and insured success in the pleading of their cases. In France, it is used as a talisman, and a child "born coiffed," as they say, need never fear to contend in games of chance, as the prize is his through power of the caul. Collin de Planey relates that when an infant was born with a caul the parents interpreted it as a sign given to them, that the child was destined for the "vie religieuse," and without any further proof the "coiffed one" was placed in a convent, and, if a girl, took the veil. By analogy, the caul was called the cloak or veil. "Il est né coiffé" is a French proverb applied to lucky people. A story is told of two priests, one a soothsayer, the other a sorcerer, who desired to possess a certain caul. Meeting one day in the Church of the Holy Spirit, they proceeded to settle the dispute in a fist-fight, and the soothsayer proving the stronger, won the caul, much to his delight. Another French writer tells how delighted the mothers were at a birth with a caul, for it indicated an easy labor. When the labor was difficult, the child was endeavoring to free himself of the membrane, and left it in the birth-canal, much as a snake sheds himself of his skin in passing through a narrow hole, in the shedding season. In England, besides its power to bring good-luck, it was especially valued among seafaring men, because of its power to ward off shipwreck, and to protect from drowning and other dangers of the sea. Cauls were carefully preserved and handed down in wills from one generation to another. In Scotland, the caul is called a holy or sely how, meaning a fortunate cap or hood, and midwives in Scotland are called "howdies" or howdy-wives. Even in Burmah, the influence of the caul is felt; but there, instead of being a talisman of the sea, it is supposed to assist in gaining the goodwill of the person from whom the owner of the caul demands a favor.

It is interesting to note that the Early Church inveighed against the power of the caul. St. Chrysos-

tom, in his Homilies, censured this "foolish belief," and Canon Balsamont relates that in his time a clerk named Petus was severely censured for having bought a caul from a wise-woman in the belief that it would bring him happiness. The wise-woman pretended to foretell the fate of the newborn child from the color of the caul. If it was red, the life was to be a happy one, but if dull and lead-colored, the future was ominous. In literature, we find mention made of the caul as far back as the sixteenth century. Claude de Malleville, born in France in 1597, speaks of it in his writings, and later, Ben Johnson alludes to it in the "Alchemist."

Further interesting details pertaining to the superstitions of the caul may be found in the following books: "Histoire des accouchements chez tous les peuples," by Gustave-Jules A. Witkowski, Paris, 1887, and "Credulities Past and Present," by William Jones, F. S. A., London, 1898.

E. L. Jefferis.

Caulophyllum.—*Blue Cohosh, Pappoose Root, Squaw Root.* The dried rhizome and roots of *Caulophyllum thalictroides* (L). Michx. (fam. *Berberidaceæ*). This is a perennial herb, with an erect, smooth stem, about fifty or seventy-five centimeters (20 to 30 in.) high, bearing a thrice-ternate leaf above the middle, and a raceme of greenish-yellow flowers at the top. The rhizome is horizontal, thick, crooked, scarred above, and covered below with numerous roots. It is a native of rich, damp woods, over most of the United States, and grows also in Japan and Manchuria. It was a favorite remedy in labor among some tribes of the North American Indians, as its vernacular names indicate.

The rhizome, four inches (10 cm.) long, and about one-fourth to two-fifths of an inch (6 to 10 mm.) thick, crooked; on the upper side with broad, concave stem scars, and short, knotty branches; externally, gray-brown; internally, whitish, tough and woody. Roots numerous, matted, about four inches (10 cm.) long, and one twenty-fifth of an inch(1 mm.) thick, rather tough; nearly inodorous; taste sweetish, slightly bitter, and somewhat acrid.

It contains twelve per cent. of resin and some tannin, a glucoside much resembling saponin, which has been called *leontin*, and a small amount of the alkaloid caulophylline.

The drug is irritating to mucous membranes, the powder being highly sternutatory. It is much like saponin in its local effects. It is recommended as a uterine stimulant, of service in parturition, and also as a stimulating emmenagogue, but there is little reliable information in regard to its action. There is no official preparation, but the fluid extract is the best form of administration, in doses of ♏ v.–xxx. (0.3–2.0).

Henry H. Rusby.

Causalgia.—A term derived from Gr. καῦσις, a burning, and ἄλγος, pain, formerly employed to denote any condition associated with a burning pain in the skin. See *Erythromelalgia*

Caustics.—Substances which destroy all tissue with which they come in contact, whether normal or pathological. Previous to the introduction of anesthesia, caustics formed a very important part of the surgeon's armamentarium. The dread of the knife was but natural, and the sufferer eagerly seized upon any means that would render it unnecessary. At that period the advantage of the knife was not so marked as it is with modern aseptic surgery. After its use gangrene and septic absorption were of very common occurrence, while the destructive action of caustics rendered the wound aseptic, and these undesirable complications more rarely followed.

One of the principal uses of caustics was in the removal of gangrenous tissue from unhealthy wounds, whether traumatic or surgical. The unhealthy granulations and necrosed tissue were thus destroyed, and as the sloughs were detached a healthy healing surface appeared. Another important use was in the removal of tumors and new growths. If they were small, one or two applications would prove sufficient; if they were of great size, the growth would be destroyed in segments by the insertion of small pieces of caustic into its substance and removing the resulting slough. In certain instances a method known as *cautérisation en flèches*, was followed. The idea was to surround the base of the tumor with small points of chloride of zinc which would separate the diseased tissue from the healthy as thoroughly as if a knife had been employed. The growth could then be enucleated and a healthy granulating surface remain. Caustics were also of use in opening deep abscesses, as they slowly penetrated into the collection of pus and left a channel for its exit. For the treatment of sinuses and fistulæ, strands of thread were saturated with the caustic and drawn through the passages.

At the present day the usefulness of caustics is very limited, but when judiciously employed, there are several conditions in which they prove of much service. Their value is recognized as an application to the surface of unhealthy ulcers, as a means of destroying the poison in septic wounds, for the removal of small growths upon the surface and upon the mucous membrane of the oral, nasal, and vaginal cavities, and for the destruction of superficial malignant growths.

The treatment of indolent ulcers and other granulating surfaces with nitrate of silver, sulphate of copper, and other mild caustics is of daily occurrence and of unquestioned utility. The caustic coagulates the granulating tissue, forming a thin covering which in a short time becomes detached, leaving a healthy surface. To destroy the poison of chancres, specific ulcers, wounds produced by venomous animals, and septic wounds, the stronger caustics are required. The part must be acted upon thoroughly and rapidly to prevent the absorption of the poison, and for this purpose fuming nitric acid, chloride of zinc, and chromic acid are some of the proper caustics to be selected. The destruction of warts, papillomata, etc., by the aid of caustics is common, and whether the frequent application of mild caustics is decided upon, or their rapid removal by the stronger caustics is adopted, the result is the removal of the growth with very little, if any, deformity. The employment of caustics in the treatment of malignant diseases was the subject of much controversy up to recent years. The ease and simplicity of removing an epithelioma of the lip or any cutaneous surface by the use of caustics are very attractive, but the frequency of recurrence and the more unfavorable condition for operation that follows cauterization, emphasize the advantage of excision. The present view of surgeons is early and complete eradication and only in rare and exceptional cases would the older method be advocated.

With modern surgical technique, there is no questioning the advantage of the knife, but certain conditions arise in which the preference may be given to the treatment by caustics. In many cutaneous cancers, lupus, nevi, papillomata, chancres, etc., especially such as are of slow growth and extend superficially rather than deeply, the employment of caustics may be more advantageous than excision.

Caustics should not be employed if any glands are involved, nor when the skin approaches closely to the underlying bone, or over eminences. Upon the soft elastic tissue of the scrotum and similar tissues they must be used with great care, as the softness of the tissue renders it more difficult to control their action.

When applied they should be kept under observation and carefully removed when the proper degree of destruction has been secured. If they are left too long in contact with the parts there will be an unnecessary destruction of tissue; if for too short a time, the effect will be inadequate and often unfavorable.

Very many substances possess a caustic action, but experience has limited the number to a few which have proved most serviceable. Of these the principal ones are the corrosive acids, alkalies, arsenic, chloride of zinc, and chromic acid. Nitrate of silver is the type of the milder caustics, which are really little more than strong astringents. (For the actual cautery see article on *Cauterization*.)

Acids.—*Nitric acid* has proved the most serviceable of all the corrosive acids and is the one most employed. It acts rapidly, destroying the integument and the tissue beneath, the depth depending upon the quantity applied. Nitric acid is not so hygroscopic as sulphuric acid, but acts in a similar manner. It abstracts moisture from the tissues and combines with the albuminous constituents, producing a dry, yellow slough, which separates in about ten days, leaving a healthy granulating surface. It is not as painful as the alkalies or some of the less active caustics, on account of the rapidity of its action. One objection to its use is its tendency to diffuse itself on the surface. To overcome this the acid has been combined with saffron, asbestos, and sulphur to the consistence of a paste, which renders it more manageable. Its action may also be limited by covering the surrounding skin with gutta-percha or some greasy substance. Previous to the introduction of curetting, nitric acid was very extensively used as an intrauterine application in various forms of endometritis. Curetting, however, has displaced the caustic and its use is now restricted to erosions and specific ulcerations. It is also employed with much success in all chancres, condylomata, etc. In the bites of rabid animals and poisonous insects and in septic wounds, its penetrating properties make it a very useful caustic. The acid is applied by means of a glass rod dipped into the acid, or of a small piece of cotton wool wrapped around the end of a probe or a splinter of wood. The part should be closely watched during the operation, and when it is sufficiently cauterized it should be washed with water or with an alkaline solution.

The Acid Nitrate of Mercury was a favorite caustic among French surgeons, but is is not much used at the present day. Its action is due to the nitric acid which it contains. In addition, the mercurial salt was supposed to supply an alterative effect. Its destructive power is not so great as that of the pure acid, and yet it is more liable to set up inflammatory action in the adjoining healthy tissues. It forms a dry, grayish-white eschar which falls off in from ten to twelve days.

Sulphuric Acid is the most powerful of the acid caustics and was formerly much employed. It has a very marked affinity for the water in the tissues, in consequence of which they are rapidly dehydrated. It destroys all the structures with which it comes in contact, and combines with the albumin and fibrin, forming a tough, structureless, black slough. This is very slowly detached and may remain adherent until cicatrization is complete. As with all fluid caustics it is extremely diffusible. This is lessened by mixing it with other substances to the consistence of a paste. Richard's paste was made with charcoal; Michel's consisted of asbestos, one part to three of acid. Syme used sawdust with the acid in equal parts.

Hydrochloric Acid has never been much employed as a caustic. It is milder than nitric or sulphuric acid and its slough is whitish and soft.

Acetic Acid is a very mild caustic. It is chiefly employed in the treatment of warts, corns, and similar superficial growths. The pure glacial acetic acid only should be used.

Trichloracetic Acid is a valuable caustic in the form of very deliquescent crystals. Its advantages are, that it does not penetrate deeply and does not produce much inflammatory reaction. It has been particularly recommended in the treatment of nevi, and it is also used in venereal warts and in superficial cutaneous growths. A crystal is placed on the part to be cauterized and there is rapidly formed a dry, white, adherent eschar which is superficial, and leaves a very slight scar which is hardly noticeable. If it is found more convenient to use it in a fluid form, a concentrated solution is formed by adding one part of water to ten of the acid. It may be conveniently applied by means of a sharp-pointed glass rod.

Arsenous Acid.—This was the caustic most employed for the destruction of cancerous and other growths. When applied to a raw or ulcerating surface, it produces an intense inflammatory reaction which terminates in gangrene and death of the part. The inflammation extends into the surrounding tissues in all directions, lessening as it advances.

Arsenic does not exercise its caustic action upon the epidermis, and when the disease is not superficial it is necessary to remove the skin by curetting or by the application of an acid or an alkali. When required for use it is diluted to the extent of one-half or two-thirds with gum arabic and moistened to form a paste. There were a number of these pastes which acquired much celebrity. *Marsden's paste* was formed of 2 parts of arsenic with 1 of gum acacia. In *Dupuytren's paste* the arsenic was mixed with calomel in the proportion of 1 part to 10 or 15. *Esmarch's paste* consisted of 1 part of arsenic, 1 part of morphine sulphate, 8 parts of calomel, and 48 of gum arabic. *Sir Astley Cooper's ointment* contained arsenic, 1 part; sulphur, 1 part; and spermaceti ointment, 8 parts. *The arsenical paste of Frère Côme* contained 10 grains of arsenic, 2 scruples of red sulphite of mercury, and 10 grains of charcoal. *Plunket's caustic* contained ranunculus acris and ranunculus flammula, of each 1 ounce; arsenic, 1 dram; and sulphur, 5 scruples—to be beaten together into a paste.

The length of time during which such a paste is to be kept applied depends upon its strength. The extent of the cauterization may be estimated by the inflammatory areola in the surrounding tissues. This should not be allowed to advance too far, as a necrosis of the part will follow. On the other hand, if the redness is not well marked, the caustic action is deficient. When the arsenic is diluted one-half, the destruction of the part is likely to require from sixteen to eighteen hours. The resulting scars are white and as a rule they are not disfiguring, unless the destruction of tissue has been great.

There is a possibility of poisoning from the absorption of arsenic, and as a precaution it is advised that not more than one square inch of surface should be covered at one time.

Recently it has been recommended that a solution of arsenic in equal parts of alcohol and water should be employed in preference to the pastes. The treatment is commenced with a solution of 1 to 150, and then the strength is increased to 1 to 80. The surface is prepared by washing and rubbing until the blood is made to appear; it is then allowed to dry and the solution is applied daily until the slough separates and the disease is destroyed. The treatment is continued for a period varying from one or two weeks to two or three months, according to the extent of the disease.

Chromic Acid.—Although slow in its action this is a very powerful and a very diffusive caustic. The pure crystals are employed or an aqueous solution of about one part in four. It produces great pain. When applied it immediately coagulates albumin, and, absorbing moisture, forms a fluid caustic, which dissolves

the tissues. It gradually forms a dry, hard, dark eschar. It is particularly recommended in bites of venomous snakes, and is used to destroy superficial and mucous growths and syphilitic ulceration.

Carbolic Acid is also a mild caustic. It is not used to cause any destruction of tissue, but is employed in the treatment of poisoned wounds, syphilitic ulcerations, and hemorrhoids. It unites with albumin, producing a dry, white, and very superficial slough. It acts rapidly and painlessly, producing an anesthesia of the spot.

Alkalies.—The caustic alkalies have all been employed to a greater or lesser extent, but potash is the most active and has been most used. Their action differs from that of the acids in that they unite with the water of the tissues and, becoming fluid, destroy the underlying parts They produce soft, gelatinous sloughs, which separate quickly and leave a slowly granulating surface. They penetrate deeply and, unless carefully applied, may cause much unnecessary destruction of tissue.

Potassa occurs as small, irregularly shaped masses, or in small cylindrical sticks, in which latter form it has been prepared for convenience of use. It is very deliquescent and, unless carefully preserved, is difficult to use. The addition of lime lessens its affinity for water. *Potassa cum calce* is made of equal parts of potassa and lime, and when moistened with a little alcohol it forms the well-known *Vienna paste*. The mixture may also be fused and run into small cylindrical moulds. This caustic is kept applied to the parts for ten or fifteen minutes, and when the paste is used the area of its action may be limited by protecting the surrounding skin with adhesive plaster. The depth of cauterization depends upon the quantity of caustic appied and the length of time it is allowed to remain. When morphine is added in the proportion of one part to three it is said to form a painless caustic. Caustic potash and gutta-percha may be melted together in equal parts to form a paste which is very convenient for use, as it may be moulded into any shape.

Soda resembles caustic potash in appearance. It occurs in masses and in cylindrical sticks. Its caustic properties are milder than those of potash. It is not so deliquescent and possesses the advantage of being less diffusible. *London paste* is prepared by mixing together, in a warm mortar, equal parts of soda and unslacked lime, and moistening the mixture with water when it is wanted for use.

Sodium Ethylate.—This salt was introduced as a caustic in 1870 by Benjamin Ward Richardson. It is a white powder which, when brought in contact with moist tissue, is decomposed into alcohol and caustic soda. It is used as the Liq. Sodii Ethylatis. This is a solution of the salt in absolute alcohol. It is a syrupy, colorless liquid, and has been recommended as a very effective and manageable caustic. It is applied by means of a glass rod, for two or three successive days, and the resulting dry eschar should not be removed until it becomes detached. It has been successfully employed in the treatment of nevi, lupus, and superficial growths.

Zinc Chloride shared with arsenous acid the greatest popularity as a caustic in the treatment of cancerous ulceration. It acts rapidly, and, being deliquescent, it may—unless its action is controlled—effect a more extensive destruction of tissue than is desired. It coagulates the albuminous tissues and in a few hours forms a dry, firm, whitish slough, which separates in about one week. Chloride of zinc is mixed with wheat flour and formed into cakes, or with plaster of Paris, which very completely limits the extent of its action. Another method is to saturate lint with the deliquescent salt and then to cut off a portion of the required shape and size.

The chloride of zinc pastes are innumerable, as the fact that it has no toxic action made it a favorite caustic with many. *Canquoin's pastes* were made in four strengths with wheat flour and water in the proportion of one part to two, three, four, or five parts of flour. *Mayet's paste* contains 8 parts of zinc chloride, 1 of zinc oxide, and 7 of flour; *Robiquet's*, equal parts of zinc chloride and flour, with gutta-qercha added to form a firm mass. In *Landolphi's caustic* the zinc chloride is combined with equal parts of chloride of gold, chloride of antimony, and chloride of bromine.

Silver Nitrate is a much weaker caustic than any of the foregoing. It has no effect upon the surface, but upon mucous membranes or denuded and granulating surfaces it causes a coagulation of albumin which results in a superficial slough. This is at first grayish-white, but becomes dark owing to the reduction of the silver. It is dry and dense. This reagent acts rapidly, without pain, and does not excite any inflammatory action in the surrounding skin. It is used in the removal of warts, condylomata, etc. It is chiefly employed in the management of unhealthy granulating surfaces, which it rapidly replaces with healthy healing granulations. The pure salt, fused into sticks for convenience of use, is generally employed. Some prefer the mitigated caustic, prepared by fusing the nitrate of silver with two parts of nitrate of potassium. A very convenient method is to cover the end of a silver probe by fusing the nitrate and placing the probe in the liquid caustic, the adhering fluid being allowed to crystallize yb exposure. Other mild caustics which resemble the nitrate are sulphate of copper, sulphate of zinc, and sulphate of alumina.

Liquid Air and Carbon Dioxide Snow have both been employed to destroy superficial growths and many reports of this favorable action have been published. They have proved of particular value in the treatment of nevi. The part is destroyed by freezing. The application is not painful but the thawing of the part that follows is sometimes accompanied by great suffering. As therapeutic agents they are of unquestionable value, but the expenses and inconveniences of preparation practically exclude them from general use. In hospital work they prove most serviceable.

Atmocausis.—This is a method of inducing a destruction of tissue by means of steam. The steam is conveyed to the part by means of rubber tubing, but it is found difficult to control and regulate the effect and the method has fallen into disrepute. It was recommended in the treatment of endometritis, but proved a dangerous procedure.

Beaumont Small.

Cauterization.—The term cauterization is as correctly applied to the use of the potential cautery or caustic as to that of the actual cautery. The term, however, is so generally associated with the latter that it is almost restricted to the use of that form of cautery. Before the actual cautery was brought to its present state of perfection, it was much less employed than the caustics.

From the earliest days of medicine to the middle of the past century very little advance was made in the development of the actual cautery. The application of heated metals appears always to have been adopted, and the irons employed for this purpose remained much the same through all the centuries. Such changes as were made were in the shape and number of the irons, or in the handles which were common to the several irons. A very crude method was the application of heated coals, and the ignition of substances on the surface to be destroyed. The latter were known as *moxa* and were prepared by saturating cotton wool with nitrate of potassium and

allowing it to dry; after which it was placed in a metallic tube with a handle, ignited, and allowed to burn down to the skin. With the introduction of illuminating gas, efforts were made to utilize it as a cautery, and instruments were made by which the jet of gas was brought in contact with the part to be cauterized.

In 1876 Paquelin introduced the thermocautery which bears his name, and it remains a favorite cautery on account of its portability and the ease with which it may be kept ready for use (Fig. 1269). The principles of this well-known appliance lie in the metal selected for the burners—these being made of platinum, a metal that becomes incandescent at a comparatively low temperature—and in the ingenious

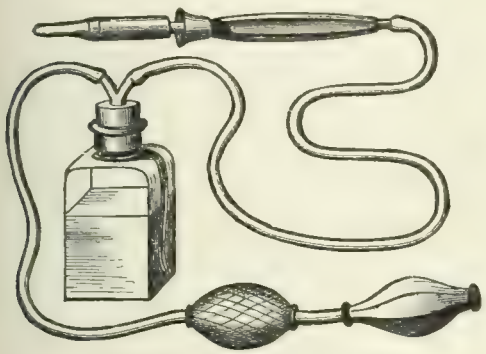

Fig. 1269.—The Paquelin Cautery.

manner in which a light benzene gas is supplied to the heated point. As long as the gas is supplied the point remains heated, the degree of heat depending upon the quantity of gas, which is easily controlled by the india-rubber bulb. Many other cauteries, based upon the same principle, have been made, but none has supplanted that of Paquelin. The electrical cautery is the most desirable at the present time, its advantages and greater conveniences being very marked. The perfection which these instruments have attained and the moderate prices at which they are supplied bring them within the reach of all.

Three degrees of heat are found desirable in the use of the actual cautery: a white heat, a red heat, and one in which the metal has not become candescent. The white heat is the most intense and the most destructive of tissue. It is also the least painful, as the terminals of the nerves are destroyed too rapidly to allow them to convey the impression of pain. The black heat is not used for cauterizing purposes, but almost solely for that of counterirritation. As a hemostatic red heat is superior to white.

The depth and extent of tissue destroyed depend upon the degree of heat and the length of time during which it is applied. It chars and destroys all tissues, and leaves a thin, dry, hard eschar, which does not become detached for several days. Ordinary hemorrhage is immediately controlled, but in the removal of pedunculated tumors, when the supplying vessels are large, it should not be depended upon. The actual cautery is employed for the removal of small tumors, hemorrhoids, and superfluous hairs, in the destruction of cancerous and unhealthy surfaces, in poisoned wounds, and in all conditions in which a caustic is desired. In the treatment of affections of the nose and throat, and in gynecological work, it is of particular service.

As a hemostatic, the actual cautery has always been of much service. In former times it was the principal means of controlling hemorrhage, and at the present day all operating rooms are provided with a cautery to check the bleeding from vascular tissues and from oozing surfaces.

As a counterirritant the actual cautery has occupied a foremost position and has proved of much service. (See also *Caustics* and *Counterirritation.*)

Beaumont Small.

Ceanothus.—*New Jersey Tea. Redroot.* The root of *Ceanothus americanus* L. (fam. *Rhamnaceæ*), a low, much and densely branched shrub of Eastern and Central North America, represented in the far West by numerous other species with the same properties. Its fruits much resemble those of the tea plant, which fact is said to have led to the use of its leaves as a substitute for tea during the revolutionary embargo. The root has enjoyed domestic and a slight professional use as an astringent. It is stout, much and crookedly branched, of a bright reddish color, which soon fades on keeping, hard and woody. The red color pervades the wood. It contains six to nine per cent. of tannin, the bark containing more than the wood. The leaves contain an equal amount. One-fifth per cent. of *ceanothine*, an alkaloid, has been reported, but nothing is known of its properties. Owing to the close resemblance, in appearance and properties, of this root to Peruvian rhatany, it has been used as a substitute and adulterant of the latter.

The dose of ceanothus is ʒ i. (4.0).

Henry H. Rusby.

Cecum and Appendix, Diseases of the. I.—The acute diseases of the cecum are clinically not distinguishable from those of the vermiform appendix. They are therefore not dwelt upon here, due attention being given them in the second section of this article on Diseases of the Cecum and Appendix. To avoid unnecessary repetition, tuberculous and cancerous affections of the cecum are also not included here, being discussed in the second part of the article.

The chronic affections of the cecum are avowedly a neglected subject of study. It is only in recent years that chronic cecal disorders were deemed of sufficient import to merit more than passing attention. This lack of interest is readily explained when we consider the star rôle assigned to chronic appendicitis during all these years.

Generally speaking, the cecum is liable to be the seat of similar chronic affections as the stomach. We may encounter chronic catarrhal states of the cecum, atony of the cecum (typhlatonia), dilatation (typhlectasia), spasm (typhlospasm), displacements, the various neuroses, etc.

On account of an anatomical and physiological relationship to the gastric organ, the cecum may fairly be designated as the second stomach. Next to the stomach the cecum is the largest pouch in the alimentary tract. Like the stomach, the cecum is a dilatation near a terminal section of the digestive canal. Both organs are receptacles for food, but while partly digested food enters the stomach from which some solids, but little liquid, are absorbed, the bulk of the digested food and nearly all the liquid transported to the cecum are absorbed by it. However, there may also be an inverse ratio, anatomically as well as physiologically, between cecum and stomach. Then the cecum may be roomy and full of tone, while the stomach is small and inactive, as is the case in certain animals, for instance, the horse and the elephant, or *vice versa*.

There still reigns much confusion about almost everything that pertains to chronic cecal disease. The clinical pictures of the various affections are neither clearly drawn nor distinctly separated from each other. The syndrome described as cecum mobile, for instance, comprises the symptom-complexes of not less than three or four different affections

of the cecum. It is a decidedly overdrawn clinical picture. Nor is the presence of a movable cecum in itself evidence of a pathological state.

In the following an attempt will be made to delineate as sharply as possible the various affections which are known to befall the cecum, and to discuss briefly their pathogenesis, symptomatology, and treatment.

Typhlatonia.—Atony of the cecum is the direct outcome of its motor insufficiency. Underlying this there may be a neurotic disposition, a wasting disease, a displacement (pathological mobility), or structural change of the cecum itself. The last two eventualities are by far the most frequent.

A displacement of the cecum, and for this reason its insufficient muscular energy, may be congenital. That which is assumed to be a neurosis may in many instances be a congenital insufficiency of the motor activity of the cecum. Displacements of the organ usually ensue with a general enteroptosis and are, therefore, most common in women who have borne children.

Typhloptosis frequently concurs with prolapsed right kidney, and it appears that the latter may be a result of the loose attachment of the right colon which, at its hepatic flexure, is connected by a ligament to the inferior pole of the kidney.

Typhlatonia is a disease entity, though, of course, it may and does occur in association with other affections of the cecum, and with such of the appendix, ascending colon, ileum, etc. To confound it, however, with so-called movable cecum, which *per se* is not a disease condition at all, means to mistake a terminal state for a possible etiological factor. There is no doubt that cecum mobile may occasion atony of the cecum, but the great majority of cases of typhlatonia have arisen in the absence of a movable cecum.

This may be the place to say a few words about *cecum mobile*. For the reason that the cecum frequently exhibits marked mobility and possesses a mesentery in common with the ileum, it is an organ favoring the location of various pathological states as volvulus, intussusception—the ileocecal and ileocolic varieties—and certain kinks, especially that of the terminal ileum (Lane's kink).

Of late a number of affections of the cecum occurring singly or in various associations with each other have been described under the collective name of cecum mobile. This attempt has not only not simplified matters, which undoubtedly was the purport of the earlier writers on the subject, but has really brought about a good deal of confusion.

In the first instance, a symptom-complex was advanced for a normally symptomless condition, *i.e.* the movable cecum; secondly, this syndrome comprises the clinical pictures of various, though often more or less coordinate affections which may be the result of different causes; thirdly, a possible causative factor of any or all these affections is being mistaken for the disease processes themselves.

The movable cecum as such is certainly not a pathological circumstance. Cohnheim regards it even as an entirely physiological condition, and Sonnenburg maintains that, inasmuch as the contents of a movable cecum are more readily removed than those of an immobile organ, the former, generally speaking, is less objectionable to its bearer than the latter. He further points out that the cecum mobile produces clinical symptoms only after it has become the seat of a catarrhal or inflammatory process, *i.e.* when a typhlocolitis has supervened. Fischler and others declare that it is not the mobility but the inflammatory state of the cecum which manifests itself clinically.

However, the question of the cecum mobile and all it implies is no longer an academic one. While it is true that we have ruled out the movable cecum *per se* as an important clinical factor, and maintain that the syndrome ascribed to it really represents the entirety of symptom-complexes of a number of cecal affections that may or may not have any connection with it, it is nevertheless true that a new era in the conception and management of many intestinal disorders has been inaugurated with the study of the movable cecum and its intraabdominal relations.

The foregoing remarks were interposed to show the true status occupied by cecum mobile in the production of cecal disease in general and atony of the organ in particular. We may take it for granted that typhlatonia is a much more frequent condition than clinically manifest movable cecum, and that the latter can only mediately be responsible for an eventually ensuing atony of the organ.

Atony of the cecum may occur with or without dilatation of the organ. The far more frequent and better-known type is the one associated with dilatation. Atony without dilatation may offer some diagnostic difficulties, because it is the enlarged cecum which furnishes most of the physical signs.

The *symptomatology* of typhlatonia, though not always uniform, may be briefly summarized, as follows: The condition prevails frequently in young individuals, but it is also common in both sexes between the twenty-fifth and forty-fifth year of life. Obstinate constipation obtaining even during the attack-free intervals is the paramount characteristic of the affection. Paroxysms of severe griping pain lasting, as a rule, for some hours, supervene at irregular periods. In a certain proportion of the cases definite paroxysms of pain never occur; the patient may experience a certain amount of discomfort, sometimes more, at other times less. There may be fulness at the site of the cecum and dragging on the ascending colon which may even be felt in the region of the hepatic flexure. Thus, the atonic cecum may readily be mistaken for a case of latent cholelithiasis. At other times the discomfort may be due to traction of the cecum on its mesentery. During an acute attack of colic there may be noted loss of appetite, often nausea and vomiting, and sometimes marked symptoms of collapse. Temperature elevation does not take place in the average case. The pulse frequency is unchanged, and the leucocyte count is normal. Palpation evinces a localized resistance or even a circumscribed tumefaction in the cecal region. The resistant area or tumefaction is never firm, but rather soft and elastic, and feels to the touch like a moderately inflated toy balloon. The palpating hands can passively displace the resistant area. Examination by the rectum does not reveal the cecal ballooning. Percussion confirms the palpatorial findings by determining a circumscribed area of tympany which corresponds more or less closely to the area of resistance offered by the distended and atonic cecum.

Ileocecal gurgling is probably the most characteristic symptom of the dilated atonic cecum; in a number of the cases cecal splashing sounds may be elicited. The palpatorial findings and acoustic phenomena are not constant during the pain-free intervals. Still, superficial resistance and cecal tympany of some degree may be educed in most, and gurgling sounds in many cases of the quiescent stage of typhlatonia.

Constipation may irregularly alternate with diarrhea during the attacks as well as in the intervening periods. Myxorrhea may occasionally supervene. Indicanuria is of frequent occurrence in typhlatonia, albuminuria is not rare during an attack, and moderate hematuria has ensued in some of my cases in which there was also prolapse of the right kidney.

Of special value in the recognition of typhlatonia, particularly when associated with typhlectasia, is the radiographic examination and the employment of Stern's procedure, viz., displacement toward the

Fig. 1

Fig. 2

Fig. 3

Fig. 4

ATONY OF THE CECUM

Fig. 1.—C., Dilated cecum; H.F., hepatic flexure of colon; T.C., transverse colon; S.F., splenic flexure of colon; D.C., descending colon; Sig., sigmoid; R., rectum; Sp., spine.

Fig. 2.—Sp., Spine; S.F., splenic flexure of colon; H.F., hepatic flexure of colon; T.C., transverse colon; C., dilated cecum; Sig., sigmoid; D.C., descending colon; R., rectum.

Fig. 3.—Sp., Spine; Cl., crest of the ilium; U., umbilicus; C., cecum; O., obstruction; Dl., dilated ileum.

Fig. 4.—S., Stomach; P., pylorus; H.F., hepatic flexure ofcolon; T.C., transverse colon; S.F., splenic flexure of colon; A.C., ascending colon; I., ileum; A., appendix; Sig., sigmoid flexure; R., rectum; D.C., descending colon; C., dilated cecum.

(DR. HEINRICH STERN—ARCHIVES OF DIAGNOSIS.)

midabdomen of the cecum, *i.e.* cecal tympany and gurgling, when the patient occupies the left lateral posture. (For details see *Archives of Diagnosis*, October, 1912.) In some cases, however, the cecum is bound by adhesions and cannot perform any excursion toward the midabdomen.

Cecal atony cannot well be misinterpreted as acute appendicitis, but it is habitually being mistaken for chronic appendicitis. The differentiation between cecal atony and chronic appendicitis, especially when the two conditions are found associated (an occurrence less frequent than commonly supposed), may be difficult or even impossible. In the general run of the cases, however, the displaceable cecal tympany and gurgling will clinch the diagnosis of typhlatonia.

Concerning the *prognosis* it may be stated that by preventing constipation the attacks of colic are generally averted or at least moderated. The atony of more recent origin, with little or no distention, may subside together with a general improvement of the organism. Older and more pronounced cases may often be rendered symptomless by appropriate treatment. Untreated or wrongly treated cases will go from bad to worse.

The *treatment* during the acute attack imperatively demands rest on the back or upon the right side with the abdomen relaxed as much as possible. This is a posture often affording relief in a short time, and it is in many instances instinctively occupied by the patient. In other cases the hypodermic administration of morphine and atropine is necessary. The application of heat to the abdomen is always gratifying. If there should not occur a spontaneous, copious evacuation of the bowels within an hour or two after the onset of the attack, a high enema of soapsuds, to which may be added some sweet oil and turpentine, should be administered. The following combinations employed as high enemata insure rapid unloading of the entire colon:

℞. Ext. colocynthidis . . . . 2 gm.
Saponis mollis. . . . 4 gm.
Aquæ. . . . . 500 c.c.

℞. Tinct. aloes . . . 12 c.c.
Olei olivæ . . . 100 c.c.
In 1,000 c.c. of soapsuds.

Prolonged rest in bed is essential if more than momentary relief, *i.e.* if the lessening of the atonic condition, is the object to be attained. From four to six weeks on the average must be devoted to this purpose. Laxatives should never be administered, neither during the period of rest nor after this when the patient has improved. The bowels should be regulated by a proper diet in which green vegetables (with the exception of the various species of cabbage), roots, oats, bran biscuits, raw fruit (especially grapes), and milk (if necessary with the addition of some alkali), should preponderate. The intake of water must not be less than 20 c.c. for each kilogram of body weight in the twenty-four hours. More than 100 c.c. of water should never be given at any one time. If the constipation persists, injections of from 100 to 200 c.c. of cotton-seed, sesame, or olive oil, slightly heated, and to be retained, may be administered every night or every second or third night. Support to the abdomen during the resting period may be procured by the proper application of strips of zinc-oxide plaster (modified Rose's belt). The cecum should be especially well supported. Later on a good abdominal supporter, fitted with a special pad for the cecum, should be worn. Excesses in eating and drinking, and mental and physical exertions must be avoided under all circumstances. Massage over the course of the colon and faradic electricity applied to the regions over the cecum and ascending colon may prove of service. The question of operating for typhlatonia and typhlectasia is still *sub judice*.

Typhlospasm.—The cecum is not infrequently the seat of a spastic condition. Typhlospasm is mostly circumscribed affecting the cecum alone; in some cases, however, other segments of the large bowel, the ascending colon in particular, are involved in the spastic state. The spasm usually causes pain, but there are authentic cases of typhlospasm in which the pain phenomenon is either absent or plays a subordinate rôle only. The spasm itself is generally of brief duration being invariably a terminal occurrence; the tendency to spasticity, on the other hand, is nearly always an enduring circumstance.

Typhlospasm occurs frequently in neuropathic individuals. Occasionally the localized spasms in women may reflexly result from disease of the pelvic genital organs. It is possible that so-called membranous pericolitis and Lane's band and kink may give rise to spasm of the cecum. In the great majority of the cases, however, abnormal absorption or fermentation processes in the cecum itself are at the bottom of its spastic condition.

Very rapid absorption of water from the cecum leaves therein a hard fecal mass which can often be dislodged only by convulsive muscular contraction of the organ. Again, the fecal mass may remain in the cecum where it undergoes abnormal processes of fermentation; the products of such fermentation may occasion spasmodic activity. We may say that spasmophilia of the cecum exists whenever liquid is too rapidly absorbed from this organ. In individuals with a physiologically overactive cecum there is always a predisposition to cecal spasticity.

Symptomatology.—In acute typhlospasm we may find the abdomen over the cecal area and possibly over that of the ascending colon distended, while it is flat and retracted over the distal portions of the colon. The spasm, however, originates in the cecum which, when containing evacuable material, looks and feels like a tumefaction; the contracted empty distal segments of the large intestine, on the other hand, impart a flat or retracted appearance to the abdomen and feel cord-like under the fingers.

The spasticity itself does not necessarily cause pain, this being entirely dependent upon the pressure or irritation of gaseous or solid material enclosed within the contracted area. The pain, when present, has its maximum intensity in the cecum and the lowermost portion of the ascending colon, whence it gradually declines. The distal half of the transverse colon is hardly ever reached by the pain-wave. The pain is always circumscribed and never has a peritoneal character. There may be a certain spasticity of the abdominal wall, especially in neurotic subjects, but the abdominal sensitiveness in typhlospasm is of a decidedly lesser degree than in peritonitis.

There is no characteristic shape of the feces in spasm of the cecum. The pencil-shaped, often canaliculated fecal masses and those resembling goat's dung attain their respective forms when passing through the sphincters. These may or may not be in spastic contraction when there is a cecal spasm, and again, there may be sphincteral spasm without synchronous typhlospasm. At any rate, cecal spasm cannot be diagnosed from the shape of the feces. The mode of defecation during the period of spasticity is rather characteristic. The patient has a desire to go to stool and makes a number of attempts at evacuation. Sometimes there will be a movement, at other times there is none. The individual movements are small. After each movement there is the feeling as if the bowel were not quite empty. There is always some tenesmus, usually more after a movement than before. The tenesmic state arises in various portions of the colon and is a manifestation of its general spasticity. If there were no spastic contractions there would be but one large movement completely evacuating the bowel. The feces are not always formed; frequently they are discharged as irregular,

thin and short, semi-solid lumps, most of which float on the water contained in a vessel while some sink to the bottom. Occasionally the movements are diarrheal and remain so for a number of days. Mucus and blood are not uncommon in the feces of spastic cecum.

Temperature elevation is never present in uncomplicated cases; pulse and respiration may be slightly accelerated during an acute spasm. Albuminuria and indicanuria, as a rule, do not ensue.

Prognostically it should be stated that acute typhlospasm is a rather short-lived phenomenon, but that latent spasticity of the cecum may continue so long as there exists colonic hypertonicity. Some cases improve or are cured when the causes which have given rise to undue physical and mental strain have been removed, others, and these are the majority, terminate in a more or less pronounced state of intestinal atony.

Treatment.—Catharsis is contraindicated in the treatment of typhlospasm as it is apt to aggravate the condition. In acute spasm nothing excels the hypodermic administration of morphine and atropine. Atropine alone will often allay the spasm. The average dose is 0.002 gram (gr. $\frac{1}{30}$); however, if opium or one of its preparations has already been employed, the tolerance for atropine is increased, and one may inject an initial dose of 0.005 gram (gr. $\frac{1}{12}$). The exhibition of atropine may be preceded or immediately followed by gastric lavage. The application of heat to the abdomen may give some relief.

When the tonic contraction of the cecum and the pain accompanying it are less marked, the administration by mouth of belladonna in combination with chloral hydrate or bromides will often render efficient service. During the latent stage of spasticity eventual neurotic tendencies should be combated. It is during this stage that the method of Albert Abrams, sinusoidalization or concussion of the spine of the eleventh dorsal vertebra for the regulation of spastic constipation, should be given a fair and prolonged trial. All efforts must be directed toward preventing an acute typhlospasm. The diet should be sufficiently bulky, but must not produce undue intestinal irritation. Large amounts of green vegetables, as spinach and lettuce, should be partaken of twice daily. A tablespoonful of olive oil one-half hour before meals and at bed-time will decrease the tendency to enterospasm in general. Cold bathing must not be encouraged, and violent exercise and sports should not be indulged in. Some individuals with spastic cecum credit flannel abdominal protectors with preventing or aborting an acute attack.

Typhlomyxorrhea.—By typhlomyxorrhea I understand the painless or painful evacuation of mucus derived from the caput coli, the cecum. Although typhlomyxorrhea, as far as its origin is concerned, is but one of the types of the condition known as membranous catarrh of the intestine, it greatly overshadows all the other location-types in frequency as well as importance. Personal experience prompts me to state that the cecum plays a more fundamental part in the etiology of colica mucosa than is generally conceded.

Typhlomyxorrhea occurs much more frequently in women than in men. It is decidedly an affection of the child-bearing period, ensuing but rarely before the twentieth and after the forty-fifth year of age. It is more common in married than unmarried women, but the frequency of gestations does not appear to have a marked influence upon its production. In every case of typhlomyxorrhea examined by me there existed typhloptosis in association with a greater or lesser degree of prolapse of the ascending colon. The displacement of the cecum was confirmed in every instance by radiography or *autopsia in vivo*, or by both. It is this invariable dislocation of the cecum that, if not directly productive, is characteristic of typhlomyxorrhea.

The glands of Lieberkühn are especially well developed in the mucosa of the cecum; they are larger and exhibit more goblet cells than those in the small intestine. To this fact must be ascribed the comparatively large amount of mucus in the greater bowel. This mucus is needed for purposes of lubrication. Deficiency of mucus may cause arrest of the onward movement of the fecal material, its superabundance may occasion diarrheal discharges.

One of the characteristic features of typhlomyxorrhea is a rather stubborn constipation that immediately precedes its onset. A tendency to coprostasis always prevails in individuals with this affection, but in a certain proportion of the cases diarrheal attacks may occasionally alternate with constipation. There is no evidence of any kind that the secretion of the cecal mucus is interfered with when constipation obtains, but there is sufficient proof that the secreted mucus may be retained in the cecum for a certain period. During this period fecal accumulation may ensue. A compensatory secretion of mucus, however, may after a while be produced by the feces which, deprived of moisture by their lodgment in the large bowel, provoke an irritation of the colonic mucosa that is followed by a more or less adequate supply of mucus. The mucus-product in these cases is therefore the result of an inflammatory process, an enteritis, and bears no relation to the normal cecal mucus.

It is possible that there may occur on the other hand an overproduction of mucus in typhlomyxorrhea. Be that as it may, there is for the time being retention of mucus in the cecum from which latter it is periodically, and often forcefully, expelled. The emission of the mucus into other portions of the large bowel is followed by its evacuation, with or without fecal material, and with or without pain. This emission *en masse* of the recently retained cecal mucus constitutes typhlomyxorrhea.

Underlying the retention of the mucus there is a malposition of the cecum and often a resulting atony of the organ. When the cecum empties itself by reason of a certain degree of (temporarily) regained tonicity, the discharge of mucus will ensue without manifestation of pain; this, however, will invariably be an accompaniment of the myxorrhea in case a convulsive contraction of the cecal muscles, a typhlospasm, acts as the expelling force. Thus, it will be seen that the presence or absence of pain in typhlomyxorrhea is entirely dependent upon the degree of cecal emissive power prevailing at the time of an attack.

The *diagnosis* of typhlomyxorrhea does not offer much difficulty. It is based upon the periodical discharge of mucus, with or without pain, and the presence of a displaced and frequently atonic cecum. Radiography is very useful in the recognition of the ptotic cecum, but not absolutely essential. The physical examination alone will mostly reveal a malposition of the organ and the substantial characteristics of its atonic state. Among the latter there is the displaced and increased area of tympany, and the acoustic phenomena emanating from the cecum.

The *prognosis* is favorable as far as life is concerned. The malady is a protracted one in many instances. The physiological decline of the organism generally brings relief. Some patients recover spontaneously; others improve under suitable treatment.

The *treatment* during the attack should consist of rest in bed, application of heat to the abdomen, especially the cecal region, and narcotics. The heat is best procured by an electric heating pad. A medium dose of an opiate to which may be added some tincture of belladonna will generally alleviate the pain. The administration of the narcotic may be

followed by an enema of not less than 250 c.c. of oil, which should be retained for as long a period as possible. On account of its antispasmodic and carminative properties camphor, preferably in the form of the linimentum camphoræ, U. S. P. (twenty per cent. in cotton-seed oil), may be added in amounts of from 10 to 25 c.c. to the 250 c.c. of pure oil. During the attacks but little food is necessary; milk and milk preparations, broths and gruels, and occasionally some whisky or brandy are permissible. Between the attacks (that is all the time when not in bed) a proper support for the relief of the enteroptosis in general and the typhloptosis in particular should be worn. A course of oil enemata according to the Kussmaul-Fleiner method, pursued for from two to four months, will frequently cause increased tonicity of the entire large intestine. Bodily exercise, if possible in the open air, should be insisted upon. A diet rich in cellulose often assists in overcoming the sluggishness of the bowels. In three of my cases of typhlomyxorrhea Wilms' method of typhlopexy—an operation that should be performed in well-selected cases only—has apparently afforded permanent relief.

Other Affections of the Cecum.—Displacements and neuroses of the cecum have been dealt with under the headings of typhlatonia, typhlospasm, and typhlomyxorrhea. The cecum is not exempt from the affections and disturbances of other portions of the large gut, thus varicoses and ulcerative processes are by no means rarities. It has been generally overlooked that it is the cecum whence an alimentary toxicosis (wrongly styled intestinal autointoxication) is often inaugurated. Absorption of toxic material from the cecum may occur very readily on account of the well-developed lymphatic apparatus of the cecum, the lymph cells of which are larger than in any other part of the intestine. Carcinoma and tuberculosis of the cecum are discussed in the following section. Heinrich Stern.

Cecum and Appendix, Diseases of the. II.—Carcinoma of the Cecum.—This is usually an adenocarcinoma. It arises from the cells of the glands and in its growth causes a diminution in the caliber of the organ and in time extends to the adjacent ascending colon and the lower end of the ileum. It is slow in growth but may reach a very large size, causing a tumor of the dimensions of a child's head which is plainly visible in an emaciated individual and can be readily palpated. The corresponding lymph glands are in time involved and adhesions take place with the omentum, parietal peritoneum, and adjacent viscera. The symptoms may be very insidious in their onset and may be those only of constipation and indefinite discomfort in the right iliac fossa. There may be at times blood in the stools and attacks of partial obstruction with tympanites, vomiting, etc. Obstruction, however, is less common here than in the lower portions of the large intestine. The *x*-ray is useful in the diagnosis and should always be employed where cancer is suspected, as in other portions of the alimentary tract.

Operative treatment offers a very good outlook when the case is brought to the surgeon. Even in cases when enlarged glands are already present and adhesions have taken place, the results of operation are often unexpectedly favorable. On this account the case should not be deemed inoperable as it would be in carcinoma of the stomach, for example, on account of immobility, glandular enlargement, and omental adhesions. The operation of choice consists in excision of the portion of intestine containing the tumor, closure of the ascending colon and lower end of ileum, and lateral anastomosis between the lower end of the ileum and the transverse colon. The operation is begun by dividing the parietal peritoneum outside and parallel to the cecum. This mobilizes the cecum; the ascending colon and lower ileum are then ligated and the enlarged lymph glands of the mesentery removed. The intestine thus being mobilized is resected between clamps and the ends of the colon and ileum are inverted and closed by means of a purse-string suture. The lateral anastomosis is made by the use of clamps and suturing is done with Pagenstecher linen thread. If the tumor is deemed inoperable on account of adhesions with adjacent organs or if there is acute obstruction present, a palliative operation may be done either to sidetrack the growth or to relieve the obstruction by means of an artificial anus. In the former case a lateral anastomosis is made between the lower end of the ileum and the transverse colon. In case of acute obstruction and dilatation a fistula will have to be established above the obstruction preferably in the lower end of the ileum. A radical operation may then be performed later.

Ileocecal Tuberculosis.—It has been estimated that eighty-five per cent. of cases of intestinal tuberculosis involve the ileocecal region and this is the sole location of the disease in six to ten per cent. of the cases. It occurs most commonly in patients from twenty to forty years of age. The infection evidently occurs from food which lies for some time in that portion of the intestinal tract. The disease manifests itself in two ways, either as a combination of ulceration and caseation or as a great hyperplasia of the bowel wall. In both cases the disease involves both the cecum and the lower end of the ileum. In the ulcerative form, fistulæ may form discharging fecal matter. There are marked adhesions and agglutination of the intestinal coils. In the hypertrophic form a tumor-like mass is formed, made up of the thickened intestinal walls and enlarged lymphatic glands. Narrowing of the lumen of the gut results as in carcinoma, although not to the same degree. The symptoms may resemble those of chronic appendicitis. There are diarrhea with blood, pain in the cecal region, and, in the ulcerative form, abscess formation and the opening of fistulæ. In the hypertrophic form the symptoms are indefinite until the production of a tumor mass in the right iliac fossa. The patient becomes weaker from the pain, diarrhea, and fever and usually dies if unrelieved by operation. It is very often difficult to distinguish between the hypertrophic form and malignant disease.

The *treatment*, however, is the same. The cecum and lower ileum are resected in the same way as described for carcinoma of the cecum. Care must be taken to remove all infected glands and to make the division of the gut at sound points which are suitable to suture. The results of operation are fairly favorable as regards both immediate mortality and freedom from further symptoms. Campiche compiled statistics of a series of 379 operations with 18.6 per cent. mortality. Of those living more than one-third remained in good health for months and even years afterward.

Appendicitis.—It was not until the year 1886 that the appendix was definitely determined to be the starting-point of the great majority of inflammatory conditions found in the right lower quadrant of the abdomen. Since that date the literature on the appendix has assumed vast proportions and the number of operations for the removal of this offending member have been legion. No other acute abdominal condition has received the attention that has been given the inflammations of this organ and no abdominal operation is so common as appendectomy or incision of an appendicular abscess.

Etiology.—Several factors, working either separately or combined, enter into the causation of diseases of the appendix. Heredity is frequently of influ-

ence. This shows itself in an abnormal structure, location, or shape of the organ, which predisposes it to inflammatory change. Thus, for example, we find in members of a family a flexion or torsion of the organ which, in the presence of other causes, will result in the occurrence of perhaps several cases of appendicitis in that family. The naturally poor blood supply of the organ is also a factor in the causation of necrosis and subsequent inflammation. If any causes accentuate this lack of blood supply, such as an acute twist, the conditions are ripe for an inflammatory invasion. The internal structure of the organ also favors infection. There is an abundance of lymphoid tissue under the mucous membrane which easily becomes swollen, occluding the lumen and thus favoring retention of secretion and resulting in inflammation. Constipation has a marked influence in the production of the disease. It favors not only congestion, but also the passage of fecal material into the appendix, resulting in fecal concretion and consequent retention of secretions. Foreign bodies are sometimes found within the appendix as causative factors but this is not of such a common occurrence as was formerly thought. Inflammatory conditions in the mucous membrane of the cecum may extend to the appendix and cause more serious results in this organ. It may be said in general that any factor which causes an interference with the drainage of the appendix into the cecum is of importance in the etiology of appendicitis. Free drainage is essential to the healthy condition of the organ and retention of secretion favors inflammation. For this reason a second attack of appendicitis is very likely to follow the first. The first attack results in permanent changes, notably a thickening, or formation of a stricture which interferes with drainage of that part beyond the stricture with consequent retention, inflammation, and perforation.

The bacteria normally present in the intestine, particularly *Bacillus coli communis*, are the most common ones associated with the infection. The usual pus organisms are often found associated with the former.

Pathology.—We divide appendicitis into two general varieties, acute and chronic. The former may be subdivided as follows:

1. Simple or catarrhal.
2. Suppurative } with or without perforation.
3. Gangrenous }

The changes in the first *catarrhal* form are largely confined to the mucous membrane. The latter is the seat of hyperemia, ecchymosis, swelling, and possibly superficial erosion. The lumen may contain fecal matter, a concretion, or a foreign body. There may be serum present. The entrance into the cecum may be closed and the organ more or less distended. The serous coat may be normal or hyperemic and be covered with a deposit of fibrin forming thin adhesions. The organ as a whole may be somewhat enlarged, firmer than usual, and adherent. The outcome of this form is either complete resolution or the appendix may be left somewhat thickened and adherent, favoring a second attack.

In the *suppurative* variety the changes in the organ are more intense. The mucous membrane is very hyperemic, swollen, infiltrated, perhaps necrotic in spots, and even perforated. The lumen will contain pus and may be closed at one point and distended beyond. The serous coat is intensely hyperemic, is adherent to the surrounding structures, and may be perforated.

The organ as a whole is greatly enlarged. The adjacent intestines are hyperemic and edematous and there may be an abscess, which is either intraperitoneal or extraperitoneal depending upon the situation of the appendix. The veins in the neighborhood may be the seat of a septic thrombus. In this variety there may be changes distant from the appendix, such as a collection of seropurulent material in the pelvis, general spreading peritonitis, subphrenic abscess, abscess in the liver or lung, empyema, etc. Finally a general condition of sepsis or septicopyemia may exist.

In *gangrenous* appendicitis the pathological changes are those of necrosis, partial or complete. The entire organ may be converted into a greenish slough. At other times a portion of the organ is so affected and the remainder shows the changes of suppurative inflammation. The gangrene is usually due to the cutting off of the blood supply from the acuteness of the inflammation or the pressure of a concretion. Sooner or later the organ perforates at the site of the gangrene allowing the escape of the contents of the appendix in the form of exudate or a concretion. The changes in the vicinity of the appendix are the same as those described in the suppurative variety and include the formation of a localized abscess or a general spreading peritonitis. The abscess that is formed in either variety may have a variety of locations depending upon the location of the appendix and may perforate in a number of directions. The usual ones are into the general peritoneal cavity, the intestine, and through the abdominal wall.

Symptoms.—Acute Appendicitis.—In the acute *catarrhal* form the patient gives a history of sudden onset often following an error in diet, exposure to cold, etc. The first symptom is pain which is sometimes felt diffusely over the abdomen, sometimes in the epigastrium or the umbilical region, and more rarely is experienced from the first in the right iliac fossa. The pain is cramp-like in character and is often mistaken by the patient or his physician for simple intestinal colic. The pain generally increases in severity during the first few hours. Following the onset of pain the patient usually becomes nauseated and may or may not vomit. It is unusual in the mild cases for the patient to vomit after the first few hours. The bowels are likely to be constipated and there is frequently some tympanites. The fever rises within a few hours to 100°, 101°, or even a little higher; the pulse may be only slightly accelerated, rarely above 100. The patient usually feels sick enough to go to bed. On palpation of the abdomen there is a sensation of muscular rigidity on the right half of the abdomen due chiefly to involuntary contraction of the right rectus. This localized muscular rigidity is of great diagnostic importance and should be carefully looked for by comparison with the opposite side. There is an area of tenderness in the right iliac fossa which may be more or less diffuse with a point of maximum tenderness at a point midway between the anterior superior spine of the ilium and the umbilicus (McBurney's point). In some cases the tenderness is located only at this point. These cases are not associated with much muscular rigidity. The rigidity may interfere with the determination of a swelling beneath the muscles but under anesthesia it may be possible to feel very distinctly an enlargement due to thickening of the appendix and matting together of the adjacent tissues, such as the intestine and the omentum. It is more often that no mass can be made out even under anesthesia. The blood count shows a varying degree of leucocytosis usually not higher than 16,000, with an increased percentage of polynuclear cells ranging from seventy-five to eighty-five per cent.

In the *suppurative* and *gangrenous* cases the symptoms above noted are much more severe. The onset is usually more sudden and stormy and from the start the patient gives the impression of being more seriously ill. The severity of the onset is often a good guide to the seriousness of the pathological changes in the organ. The cases associated with total gangrene may begin with a distinct chill. The pain, tenderness, and muscular rigidity are more

marked and nausea and vomiting are more constantly present. The temperature is on a higher level, reaching 101° or 102.5°, and the pulse rate rises to 110 or higher. The right thigh is often drawn up by the patient to relax the psoas muscle. On palpation the local muscular rigidity is found and after a few hours a mass can often be felt through the tense abdominal wall. This mass is due to the enlarged appendix alone or combined with the matted intestines and omentum, or to an abscess outside the appendix either intraperitoneal or extraperitoneal. The size of the mass has thus wide variations and if caused by an abscess may reach an enormous size. Ordinarily the mass can be felt from in front by the palpating hand, and when large gives dulness or flatness on percussion. In the retrocecal variety the mass may not be palpable except by placing one hand in front and the other behind so that the tumor is brought between the two hands. Failure to resort to this procedure will often cause the physician to overlook the presence of this variety of abscess. If not promptly evacuated the abscess may give rise to a gradual spreading of the infection to the rest of the peritoneal surface, causing in time a diffuse peritonitis. If the abscess ruptures into the general cavity a rapidly spreading peritonitis results, which will prove fatal unless promptly treated by operation. This rupture is associated with sudden tearing pain, subnormal temperature, and diffusion of the abdominal symptoms over the whole abdomen. The most common cause of general peritonitis is suppurative appendicitis and a large percentage of the cases of the latter will go on to peritonitis if left to themselves. Hence the importance of early recognition and early operation in appendicitis. It is furthermore important to remember when a case of general peritonitis presents itself, that the appendix is the most common starting-point and hence the abdomen should be opened near the same so as to remove the diseased organ as the first step in the treatment. The fully developed peritonitis is easy of recognition. It is the progressive variety that may elude the observation of the physician, so gradual may be the spreading of the process from the localized area. Careful examination of the patient should in most cases lead to a correct diagnosis of a spreading infection. The patient begins to look sicker, the abdomen frequently becomes more tympanitic, and vomiting which may have ceased after the onset of the attack usually begins again and is more marked. The abdominal rigidity which was before localized now becomes more diffuse and the same is true of the tenderness. The patient complains of a more general pain in the abdomen and may lie with both knees flexed. The temperature rises to a point two or three degrees higher than before, and, what is most important from a diagnostic standpoint, the pulse rate rises and may reach 130 to 150. The leucocyte count also rises in the cases showing good body resistance and the percentage of polynuclear cells is very high—eighty to ninety per cent. The patient becomes progressively restless and the respirations are rapid and more superficial.

Treatment.—The treatment of the simple *catarrhal* cases may be expectant and symptomatic. An ice-bag is applied to the right side of the abdomen or if heat is preferred, a hot-water bag or stupes. The ice is preferable if well borne. The bowels may be moved at the onset by calomel and salts, but later it is better to use a daily enema. The patient is put upon a fluid diet, and is kept in bed until the pain, tenderness, and rigidity have disappeared and the temperature and pulse are normal. The question of operation will come into consideration in these mild cases. If the patient is seen during the subsidence of the attack it is well to wait, and then advise him to have the appendix removed after the attack is over and before another attack occurs. If seen at the outset, and the diagnosis is sure, I believe that the safe course is to have the operation done, as one is not sure what the next hours will bring. It is unquestionably safer to operate at once than to run the risk of a rapid course with perforation, spreading peritonitis, etc. A mild onset may mean a mild course, but this is not always the case, and what was thought a simple catarrhal case may develop into one of a severe type.

The danger from early operation is certainly less in the long run than that from the expectant method of treatment.

In the *suppurative* and *gangrenous* cases we should operate when the case is first seen, whether in the first hours of the attack or at the expiration of days. The severity of the onset is a good guide as a rule to the seriousness of the pathological changes in the appendix. If the patient has very intense pain, a chill, an unusually high temperature, marked local rigidity or local tenderness, and an excessive degree of vomiting, or appears very ill we should expect to find a badly inflamed or damaged organ. The presence of one of these factors in an exaggerated form should impell us to immediate operation. A great advantage of early operation from a technical stand-point is the simplicity of the procedure as compared with the difficulty in cases which have gone on to perforation or marked adhesions of the organ to adjacent structures. If removed early, the inflamed and swollen appendix can simply be tied off, the stump cauterized or infolded, and the abdomen closed without drainage. If perforation has occurred it will be necessary in addition to drain the abscess cavity for a longer or shorter period. In one case the patient may leave the hospital in a week or ten days, in the other case he may be confined to bed for weeks and the sinus may not close for months.

Technique of Operation.—The location of the incision depends upon the method employed in dividing the muscular wall. In case of the McBurney or gridiron method the skin incision should cross the line from the anterior superior spine of the ilium to the umbilicus at a point about one and one-half inches from the anterior superior spine and should be two to three inches in length. The aponeurosis of the external oblique is divided in the course of its fibers and then the internal oblique and transversalis muscles are split in the course of their fibers which run at right angles to the incision through the skin and aponeurosis. The transversalis fascia and peritoneum are finally divided and the abdomen opened.

In the cases without perforation or an abscess the appendix is found by following down the anterior band of the cecum to the base of the appendix, the rest of the intestines being if necessary held out of the way by pads or packing gauze. The free margin of the mesentery of the appendix is held by an artery clamp and the mesentery tied off in sections with plain catgut, on a ligature carrier, until the cecum is reached. The appendix being now free is crushed near its base by a clamp and ligated at the crushed portion with plain catgut. The cut end is cauterized by means of pure carbolic acid followed by alcohol or by means of the thermocautery. It is sufficient to allow the stump thus sterilized to remain free or it may be turned into the cecum by inversion and secured by a purse-string stitch, or the cut edge may be covered by a cuff of peritoneum. The abdomen is then closed without drainage provided no necrotic tissue at the stump or elsewhere is left behind. In cases where an abscess is present the latter is located, the intestines walled off to prevent contamination, and the pus allowed to escape on stick sponges until the cavity is empty. If the abscess is a fresh one, *i.e.* of a few days' duration, it is usually safe to search for the appendix and remove the same in the way just described. In an abscess of some standing, *e.g.* ten

days or longer, it is safer simply to drain the abscess cavity without attempting to remove the appendix, which is usually hemmed in by adhesions, the breaking through of which might cause a spreading of the infection to the unsoiled peritoneum. Under these circumstances, drainage alone is employed. In many such cases the appendix has already sloughed away. It may heal up and give no further trouble, while in other instances it may require a second operation for its removal. The important thing in these cases is to save life, not risk it by doing too much, and leave the question of dealing with the appendix to a subsequent time.

For drainage purposes rubber tubing is the most desirable form when considerable pus is present or expected during the subsequent course. This may be used alone or with a piece of gauze inside the tube and projecting from both ends. As soon as the pus diminishes in amount, a piece of rubber tissue, enclosing a gauze wick (cigarette drain) may be substituted. In most of the early cases where an abscess has not had time to form, and yet the stump contains necrotic or infectious material, the rubber tissue drain is the method of choice. Complete closure of the cavity without drainage is proper only when no necrotic or infected tissues are left behind in the stump, omentum, etc. After leaving the operating table, the patient should be given, in all suppurative cases, some form of saline administration by rectum. The most efficacious is the Murphy drip method, which may be kept up for several days with intermissions. Pain may be combated with small doses of morphine during the first twenty-four hours. The rectal tube or an enema aids very materially in reducing the discomfort from gas. Bowel movements should be secured at first by enema and later some form of catharsis is allowable, preferably calomel and salts. Cases that are complicated by peritonitis require special measures to combat the general as well as the local inflammation. The first indication is to remove the infected appendix as above described and then to proceed to get rid of the purulent exudate. In the earlier stage when the latter is confined to the pelvis it may be sufficient to sponge it out with gauze. When it is disseminated through the abdominal cavity sponging is unsatisfactory and resort may be had to irrigation with saline, or to aspiration by means of a suction apparatus. For irrigation purposes a Blake tube is very useful as it allows the introduction and removal of the saline solution to be accomplished in the various localities of the peritoneal cavity where the pus is most abundant. Such localities are the pelvis, the right and left gutter outside the ascending and descending colon, the upper surface of the liver, etc. A modification of the tube can be used in connection with a suction apparatus. The important point in the evacuation of the pus is to avoid undue exposure and manipulation of the intestines. Such exposure and manipulation not only add very seriously to the shock from the operation, but also damage the serous surfaces, thus diminishing the absorption power of these surfaces and the elimination of the poisonous products within the cavity. Neglect of this precaution will sacrifice many a life which would have been saved if too rigorous an attempt had not been made to get rid of every drop of pus. The peritoneal surfaces are able to take care of considerable purulent material and hence they should be relied upon to do so.

The one important thing is not to injure these surfaces and thus reduce their absorbing power. The surgeon who fulfils the main indication without unnecessary prolongation of the operation or undue exposure of the intestines will get the best mortality results. The radical methods formerly employed had a very high mortality, and have been properly superseded by the simpler and shorter procedures. An incision three inches in length is sufficient to carry out all the necessary procedures of the simplified technique and insures not only a low mortality but also stronger and less disabling scars. As a general rule it is not necessary or advisable to drain in cases of peritonitis to any further extent than the appendix region requires. A separate drainage tube running down into the pelvis does, however, no harm and may be useful in washing out later any accumulation of pus in the pelvis. The use of counterincisions in the opposite flank, or of rectal or vaginal openings is very seldom necessary and it is to be avoided on account of prolonging the time of operation.

After operation the patient is given saline by rectum, preferably in the form of the Murphy drip. The Fowler position in which the head of the bed is raised two or three feet is of undoubted value in causing a gravitation of the fluid left in the abdomen toward the pelvis drain. The bowels are moved by high enemata of ox-gall or turpentine and as soon as the patient's stomach will tolerate it, calomel is given followed by salts. Should the distention be extreme, and the bowels not move in spite of repeated high enemas and catharsis, incision of the intestine may be considered for relief of the distention and escape of intestinal contents. The mortality of operation for general peritonitis following appendicitis has been lowered within the last few years very materially and largely through the introduction of the methods of operating just given.

Chronic Appendicitis.—As the result of repeated attacks of the milder forms of appendicitis a chronic condition of the organ follows. Each acute attack results in further change in the organ already damaged by the first attack. The mucous membrane of a chronically inflamed appendix shows often atrophy and cicatrices. The result of the latter is stricture of the lumen, causing retention of secretion. The portion below the stricture may be dilated and contain old pus or an enterolith. There may be a concretion at one point which likewise causes interference with drainage. There are frequently extensive adhesions about the organ, binding it to adjacent structures such as the cecum, omentum, small intestine, ovary, etc. The wall of the appendix is thickened and the lumen may be completely obliterated.

The *symptoms* produced by such an appendix appear either in the form of attacks with a free interval of health or the patient may have constant digestive disturbances of a local or general character. He suffers from local discomfort, flatulence, constipation, and general ill health. When the appendix is the cause, removal of the same will cause a rapid disappearance of the symptoms and may restore the individual to perfect health, who had been for years a chronic invalid with dyspeptic symptoms. The operation in these cases is very simple and corresponds to that for acute catarrhal appendicitis. No drainage is necessary as a rule and the patient is often up and about on the eighth day. By way of differential diagnosis it may be stated here that many cases supposed to be chronic appendicitis on account of the location of the pain and other disturbances in the right iliac fossa are in reality cases of displacement or abnormal mobility of the cecum alone or also of the colon. Ptosis of these organs, with or without movable kidney, is a very common condition especially in the young undernourished female.

Removal of the appendix in these cases often shows it to be normal, and the expected beneficial effect of the operation is not obtained. On the other hand it is equally true that an appendix which at first sight appears to be normal, may be found on more careful examination to have certain pathological changes which caused the symptoms referable to it. Morris has shown that the nerve-endings in the appendix may be compressed by abnormal involution of the organ thus causing severe pain or neuralgia and reflex

disturbances of digestion. It may require the microscope to detect the anatomical changes in the wall of the appendix but removal of such an organ often results in complete disappearance of the abdominal symptoms.

There are certain factors which influence and modify appendicitis and deserve consideration even in a short treatise on the subject. These are, childhood, typhoid fever, and pregnancy.

Appendicitis in the Child.—So far as frequency is concerned the disease is very rare under the age of five, but its frequency increases greatly after that year and it is extremely common between ten and fifteen. In regard to etiology, round worms undoubtedly play a rôle in children which is not the case in adults. In a boy of ten I found three large round worms in an appendicular abscess. One of these was alive.

The symptoms of the disease in children are often very vague. The child does not localize the pain and tenderness with sufficient accuracy in most cases to make the diagnosis easy before a definite mass is palpable in the right iliac fossa. Sometimes the child, if carefully watched, will be observed to keep the hand on the right side of the abdomen. Examination per rectum is of help in children for the purpose of making out a mass in the pelvis. In the early stages it is very easy to mistake for acute appendicitis several acute conditions which are associated with abdominal pain. Such are the onset of pneumonia, the infectious diseases, particularly scarlet fever, and typhoid, acute indigestion, intestinal obstruction, and coxitis. All of these conditions should be thought over carefully before the diagnosis of appendicitis is made and an operation advised. After the formation of a psoas abscess in connection with Pott's disease the error is often made of mistaking the abscess for suppurative appendicitis. Reliance will have to be made here upon the history of the onset, the presence of pain in the spine or a kyphosis, and the prominence of abdominal or intestinal symptoms. The treatment of acute appendicitis in children does not as a rule require the promptness that is so often essential in the adult. In other words the waiting policy will on the whole give satisfactory results. If there is any doubt of the diagnosis it is far better to wait until the local signs are unmistakable. It will then be possible to avoid the error of operating upon a case of pneumonia or pleurisy, acute indigestion, and the other conditions enumerated above, which have been so often confused with appendicitis. The child does not suffer from delay in operating to the same extent as the adult. On the other hand abdominal section for pneumonia or other acute infectious disease may have very disastrous results. Even the neglected cases of large appendicular abscess and of general suppurative peritonitis in children show a very low mortality in good hands. The technique of these operations has been so improved and the child's natural resistance is so good that deaths after operation in children are very exceptional.

Appendicitis and Typhoid Fever.—The differential diagnosis of these conditions may be difficult. Many cases of typhoid show at the onset marked abdominal symptoms sometimes referable to the right iliac fossa. This has led in many cases to operation with the removal of a normal or congested appendix, and the patient has then gone on to a typical attack of typhoid. Such a mistake brings discredit upon the physician and may seriously complicate the case. The high fever, the more marked prostration, the headache, and the slower onset are important diagnostic points favoring typhoid.

During the course of the typhoid fever when there is no doubt about the nature of the disease it is possible for an appendicitis to develop of a mild or severe degree. This may be a mere coincidence or may be due to typhoid ulceration in the appendix with local signs of appendicular inflammation or perforation. It may then be a doubtful question between perforation of the ileum and appendicitis. It is wise in these cases to be conservative if the diagnosis of appendicitis is made. Abdominal section in the course of typhoid is a serious matter and should be done only in the presence of a definite indication. The mere diagnosis of an inflamed appendix is not sufficient. It must be evident that the condition of the appendix is a real menace to the individual and that allowing it to remain would be more dangerous than its removal. If operation is done the shortest possible time should be consumed, with the least handling of the inflamed intestines.

Appendicitis and Pregnancy.—It is doubtful whether the condition of pregnancy has any etiological bearing upon the development of appendicitis. Appendicitis is such a common disease in the child-bearing age that it is not surprising that many cases develop during the months of pregnancy. It is possible, however, for an appendix which has been the seat of antecedent inflammation to have formed adhesions in the vicinity of the enlarging uterus with the result that a fresh attack is brought about by the new conditions in the pelvis. If the patient has a bad attack during pregnancy and is not operated upon before delivery it is possible that the violent contractions of the uterus or the sudden diminution in its size after delivery may have a very disastrous effect upon the local focus about the appendix. This may mean not only a stirring up of the disease but an actual rupture either of the appendix or of a periappendicular abscess with rapidly spreading peritonitis. As regards the effect of appendicitis upon the pregnancy it has been found that premature delivery has occurred in many cases with no untoward effects upon the child. In case of premature delivery associated with septic peritonitis death of the fetus and the mother might be expected.

The *prognosis* of acute appendicitis in the pregnant woman has therefore to be given guardedly and the question of operation is a most important one. The earlier the attack occurs in the course of the pregnancy the better the prognosis. Operations at an early stage would have the advantage of freeing the individual from a possible menace at the time of parturition. If the attack occurs late in the pregnancy we must be guided by the severity of the attack in regard to operative interference. A mild attack can safely be allowed to subside and operation postponed until later. In case of a severe attack early operation would be the safest plan as no risk will then be run of abscess formation or general peritonitis, both of which may be fraught with most serious consequences both for the mother and the child. Cases of intermediate severity require great judgment but here one should lean rather toward radical than conservative measures as one is not sure just how seriously the appendix is involved and how much infectious material may be left behind after an apparent cure. A small infectious focus can be lighted up after the act of parturition and a rapidly fatal result may ensue. To avoid this great risk the lesser risk from a premature delivery should be assumed. A skilful operation should prevent in most cases premature delivery as there would be very little handling of the intestines or other traumatism to produce uterine contractions. If a serious attack develops in the days following delivery prompt measures are necessary as the prognosis is very bad from delay. Such cases often mean that an appendicular abscess has ruptured on account of the sudden diminution in the size of the uterus which may have formed part of the protecting wall of an abscess.

Carcinoma of the Appendix.—This is usually primary and occurs in young subjects most commonly of the female sex. It is closely allied to chronic inflammation of that organ. MacCarty and McGrath have shown from a study of 5,000 appendectomies that cancer occurs once in every 225 cases of chronic appendicitis. In some cases the tumor has been situated at a point of stenosis resulting from several attacks of appendicitis. It is a well-known pathological fact that carcinoma is prone to develop in atrophic or rudimentary structures of which the appendix is a good example. The irritation from a concretion or other foreign body might theoretically have some etiological bearing on the development of carcinoma but such a relationship, as in gallstones, has not been established probably because the appendix concretions are not so irritating to the mucous membrane as gallstones.

The age of the patient in whom a carcinoma of the appendix has been found at operation or autopsy is usually under thirty. This age corresponds very closely with that of acute inflammation of the organ.

The clinical signs of carcinoma of the appendix are not as a rule characteristic and have not in the past been sufficiently differentiated from chronic inflammation to make possible a diagnosis between the two conditions before operation. If the carcinoma causes perforation of the appendix the usual symptoms of perforative appendicitis will ensue. In case a large mass results from the growth differentiation may be hard to make from an appendicular abscess of long standing, as well as from a carcinoma starting in the cecum. The cases thus far operated upon have shown a decidedly favorable outcome as regards recurrence. In fact local and general metastases seem to be long delayed and the tumor in other respects runs a more benign course than those in other parts of the intestinal tract. With the increasing tendency to operate early for appendicular symptoms more cases of carcinoma will come to light and the patients will be operated upon at an early stage before the tumor has reached a large size or involved adjacent tracts.

Sarcoma of the Appendix.—This is very rare and only isolated cases are found described in medical literature. There are no special features which make it possible to differentiate this tumor from carcinoma. Sarcoma also occurs most commonly in young subjects.

Benjamin T. Tilton.

Cedar Keys.—A small town of about 2,000 inhabitants, situated upon the gulf side of Florida, 155 miles southwest from Fernandina, with which it is connected by railroad. As will be seen from the accompanying climatic chart, the climate is a mild equable marine one, with a large number of clear and fair days:

The winter climate is said to be milder than that found upon the east, or Atlantic, coast of Florida. The facilities for bathing, boating, and hunting are also said to be good. So far as climatic conditions are concerned, Cedar Keys differs but little from Tampa, about 100 miles farther south on the same coast, but the former has not become a "resort" like the latter, and has no such accommodations as exist at Tampa. The drainage and water supply are also said to be questionable. Although Cedar Keys is reputed to be "extremely healthful," one would hardly care to send an invalid there unless he were sure of obtaining adequate accommodations and favorable hygienic conditions. These latter are quite as essential as a favorable climate in the selection of a health resort.

Climate of Cedar Keys, Fla. Latitude, 29° 8′; Longitude, 83° 2′; Period of Observation, Four Years.

Data.	December.	January.	February.	March.	Year.
Temperature (Fahr.)—					
Average or normal	59.5°	59.8°	62.0°	63.9°	71.3°
Average daily range	12.1°	12.1	12.2	12.5	
Mean of warmest	65.6	64.4	68.8	71	
Mean of coldest	53.5	52.3	56.6	58.5	
Highest or maximum	78	77	79	82	
Lowest or minimum	22	32	35	40	
Humidity—					
Average relative	80.8%	81%	75.4%	71.5%	75.4%
Precipitation—					
Average rainfall in inches.	2.73	5.31	2.98	3.58	58.02
Wind—					
Prevailing direction	N.E.	N.E.	N.E.	S.W.	N.E.
Average hourly velocity in miles.	8.5	9	9.6	11.1	9.2
Weather—					
Average number of clear days.	14	8.5	13.8	14	158.4
Average number of fair days.	11.4	14.7	9.2	12.2	149.4
Average number of clear and fair days.	25.4	23.2	23	26.2	307.8

Edward O. Otis.

Cedron Seeds.—The seeds of *Simaba cedron* (P. Br.) Planch. (fam. *Simarubaceæ*). The plant is a small tree of Northern South America, and is considerably cultivated in the tropics. It yields an edible fruit about the size of, and somewhat resembling, a large peach. The solitary seed is similar to a Brazil nut in both form and size. In their home, the seeds have a high repute as an antiperiodic, and trials with them here have largely supported these claims. Their use as an alternative of the cinchona products appears well justified. The white or whitish crystalline volatile amaroid *cedrin* appears to be the active constituent, though the presence of an alkaloid has been claimed. Cedrin is soluble in both water and alcohol. Cedron seed is commonly given in the form of the fluid extract, the dose of which is ♏ i. to viij. (0.06–0.5).

Henry H. Rusby.

Celandine.—See *Chelidoneum*.

Celery.—This well-known succulent vegetable, *Apium graveolens* L. (fam. *Umbelliferæ*), is distilled in the fresh state for a delicious volatile oil which is used for flavoring. The fruit, however, is the important part from the standpoint of materia medica, and is recognized in the National Formulary. It is similar to the other cremocarps of the family, but is very small, only one-twenty-fifth inch in length, broadly ovate, dark brown, hard and smooth. In the cultivated garden varieties, each mericarp has ix unbranched oil tubes, but in the wild state these are making two-forked near the base. It is largely used in its own form for flavoring purposes and as a carminative, similarly to its relatives, and in doses of ʒ ss. to i. (2.0–4.0). Its volatile oil, containing limonene, is also largely used for the same purposes.

Henry H. Rusby.

Celiac Disease.—This condition, also known as morbus cœliacus, belly affection, and acholia, was first described in 1888 by Samuel Gee[1] under the name "celiac affection," from the Greek κοιλία, meaning belly. The ancient writers, Aretæus and Aurelian, had however, referred to probably the same condition

under the term "celiac diathesis." Gee defines celiac disease as a form of chronic indigestion that occurs at any period of life, but chiefly between the ages of one and five years, the largest number of cases occurring during the second year of life. Its most conspicuous manifestation is the condition of the feces, which are loose but not watery, pale, yeasty, frothy, or of an appearance somewhat like that of oatmeal porridge. Another characteristic of the stools is the stench, which is the result of putrefaction. The color may vary from a pure white to a dirty drab, and there may be sometimes a slight yellowish admixture. These appearances are due to the marked diminution or complete absence of bile. The so-called "diarrhea alba" of India is referred to as a similar condition. The term "diarrhea chylosa" was also formerly applied to this group of cases. Englishmen returning from India sometimes bring this disease back with them. Diarrhea alba may however occur in adults who have never been outside of England. The causes of celiac disease are obscure. Children affected with it are not all weak. As regards the etiological influence of errors of diet, it is noted that among the children of a family all of whom eat the same food, one child may develop celiac disease while the others may be free from it. No definite pathological changes have been discovered. The onset of the disease is as a rule gradual. But it may start suddenly like an accidental diarrhea. Wasting is a conspicuous manifestation, being more pronounced in the limbs than in the face. There is great muscular weakness, and occasionally muscular tenderness. Cachexia is constant. There is marked pallor, and edema of the limbs may be present. The spleen is sometimes enlarged. The patient's loss of color resembles that of splenic disease or of malaria. The abdomen is soft, doughy, and inelastic, and sometimes distended and tense. There nay be flatulence. The appetite is variable. In some cases there is an evening rise of temperature. The three pathognomonic features of this disease are the diarrhea alba, the emaciation, and the cachexia. Ulceration of the intestines may produce all the features of celiac disease. In children chronic ulceration of the intestines is often tuberculous or syphilitic, and but seldom dysenteric. The diagnosis of ulceration hangs upon the presence of a considerable amount of pus in the stools.

The course of the disease is slow. It may last months or years. Death is the common termination, resulting usually from some intercurrent disorder. Recovery may be complete or incomplete. In the former case the patient is left with a weakness of the limbs which is observed after all other tokens of the disease have disappeared. There is a tendency to relapses. While the disease is active the child ceases to grow; even on recovery it is left frail and stunted.

The *diagnosis* of celiac disease rests upon the recognition in a child usually under five years of age, of the following group of symptoms: the large, acholic, and fetid stools; the distended abdomen; the emaciation; the cessation of growth; and the pallor. The chief difficulty in the diagnosis is the exclusion of tuberculous peritonitis which may be accompanied by most or even all of these symptons. Prolonged observation, and the performance of the diagnostic tests for tuberculosis will eventually enable one to decide whether or not the case is one of tuberculous peritonitis. The development of ascites or the presence of enlarged mesenteric glands will remove any doubt as to the tuberculous nature of the condition. The enlarged abdomen of rickets, of Hirschsprung's disease, of splenomegaly, of hepatic cirrhosis, and of chronic intestinal indigestion may simulate that of celiac disease. The diagnosis of intestinal infantilism, which further study may show to be identical with celiac disease, depends upon the identification of the characteristic microorganisms in the feces.

The *treatment* consists chiefly in regulation of the diet. Cows' milk is least suited for these cases, but asses' milk is well borne. If the latter cannot be obtained, one may use whey, or cream and water. There should be only a small allowance of farinaceous food. The skin should be kept clean and warm. Fresh air is necessary, but muscular exercise is not to be indulged in. The drugs recommended are carbonate of bismuth and aromatic chalk powder, and occasionally a dose of the compound decoction of aloes.

The use of bismuth and soda for the looseness of the stools, of salol and the sulphocarbolates for the putrefaction, and of chloral and bromides for the nervous irritation; and the administration of hepatic stimulants, such as brandy, tincture of podophyllin, sodium salicylate, and ammonium chloride are advised by Cautley.[7] This observer also suggests that glycocholate of sodium may be tried, as the bile salts stimulate biliary secretion; that small doses of gray powder are useful, and that iron and arsenic may be administered during convalescence. He also notes that codliver oil is generally injurious, and that the seaside is rarely beneficial. If future observation reveals the identity of celiac disease and intestinal infantilism, then a rational mode of treatment would be the administration of a vaccine made from the alleged causative bacteria. Freeman refers to the good effects noted by Bramwell in a case of this nature by the administration of pancreatic extract. This method of treatment would also be justified on the basis of the observation, already mentioned, of a case of obstruction of the pancreatic duct, in which the clinical picture was one of celiac disease. Whipham[8] recommends that the colon should be irrigated once or twice daily, and that abdominal massage may be employed later as the condition improves. Goodhart and Still[9] allude to the beneficial effect of a restricted diet, particularly the limitation of fats and carbohydrates, and to the use in obstinate cases of peptonized foods.

Acholia.—W. B. Cheadle[2] describes the same condition under the name "acholia." He points out that minor degrees of this affection are not uncommon. Only the severe forms are rare. The disease, though serious, is seldom fatal. The main characteristic of the affection is the absence of bile from the feces. At the same time there is no jaundice. Sir Joseph Fayrer has described a similar condition of the stools in the white diarrhea of the tropics, and P. Manson and G. Thin have noted the same condition in sprue. T. J. Walker[3] reported two cases of complete obstruction of the pancreatic duct, in one of which a condition of colorless stools persisted for more than twenty years. These cases occurred in adults over fifty years of age. The white diarrhea of the tropics is also a disease of adult life. Cheadle describes the stools in acholia as pale, fawn, clay, or straw colored, having the appearance of putty or of white paint. In the differential diagnosis of acholia it must be borne in mind that white stools may be caused by a number of other conditions. Temporary white stools may be the result of dietetic excesses, gout, and chronic nephritis. Diarrhea alba and sprue must also be ruled out. Infants fed exclusively or chiefly on milk also have light stools, but these have a yellowish or brownish tint. The typical acholic stools are dirty gray or white with the absence of any yellowish tinge. They are greasy, glistening, and fatty; are extremely offensive; and are voluminous. The disease may set in gradually or abruptly. At first there may be a rise of temperature, especially if there is difficult dentition. But the temperature may be normal or subnormal. The child has no appetite and is pallid, languid, and enfeebled. In one case in which the stools were analyzed, these showed in addition to the characteristic appearances above described, the following changes: They were slightly alkaline and contained 85.46 per cent. water. The dried feces consisted almost entirely of

fat. Normal feces contain only from twelve to sixteen per cent. of fat.

Cheadle notes that the pathology of this condition is extremely obscure. A number of possibilities suggest themselves. Acholia may be due to the absence of bile, to the absence of bile pigment, to the fact that although the bile may enter the intestine it may be subsequently absorbed, or to the fact that the bile pigment may be so changed in transit through the intestine that it fails to color the feces. Walker, on the basis of the pancreatic duct obstruction found in one of his cases, suggested that there is some defect in the transformation of the biliary pigment, so that this is not converted into the hydrobilirubin of the feces. He believes that this transformation is normally effected by the pancreatic secretion, and that the absence of the secretion accounts for the absence of the normal color of the feces. Cheadle does not accept this explanation, for he has found that the administration of bile to patients suffering from acholia gives rise to the passage of greenish stools. He believes that in these cases the function of the liver and possibly also of the pancreas is interfered with. He bases this theory upon the following facts: the stools are greasy, acid or slightly alkaline, and extremely offensive, which changes can be accounted for by the absence of bile and of its antiseptic influence; the stools are large on account of the imperfect digestion and absorption of fat; and the patient is emaciated and anemic in consequence of this defective digestion and absorption of fat. In one of Cheadle's cases there was a defective elimination of urea, the urine containing only 0.45 per cent. of this substance, and an excess in the number of leucin crystals in the urine. Postmortem examination in these cases reveals no abnormality in the liver, although in some cases there is an enlargement of the spleen. In sprue there have been described necrotic erosions of the mucous membrane of the stomach and intestines. Manson believes that these erosions are secondary to starvation. Gibbons advances the theory that acholia is of nervous origin, basing this view upon the recognized influence of the nervous system upon glandular secretion. Cheadle regards acholia as the result of a dental irritation reflex or of a surface chill. In the treatment he recommends the use of predigested starches, broths, beef tea, fresh meat, skim milk, malted bread and biscuits, and fresh fruits. The looseness of the stools is to be controlled with opium and bismuth. The chloride of iron with arsenic has a good tonic effect in these cases. Brandy in doses of ten to sixty drops is an effective hepatic stimulant. G. F. Still[4] questions whether the absence of bile from the stools should be regarded as a disease *sui generis*. He believes that this deficiency is rather a symptom of indigestion in infancy and childhood.

Intestinal Infantilism.—In 1908 C. A. Herter[5] described a form of infantilism, which he termed intestinal infantilism. (See *Infantilism.*) There is such a striking similarity between the cases belonging to this group, and the cases of celiac disease described by earlier writers, that one is inclined to regard the two conditions as identical. The symptoms of intestinal infantilism are an arrested bodily development with slight mental retardation; marked abdominal distention; a mild degree of secondary anemia; pronounced bodily and mental fatigue following slight exertion; and a tendency to looseness of the stools, which are acholic and of grayish color and contain an excess of fat, and a large amount of fatty acids and soaps. The ordinary bacteria are absent from the feces in these cases. Gram-positive microorganisms predominate. The principal bacteria present are the *Bacillus bifidus* of Tissier, the *Bacillus acidophilus* and the *Bacillus infantilis*. There are characteristic changes in the urine which is increased in amount and contains an excess of ethereal sulphates and large amounts of aromatic oxyacids. No satisfactory explanation of the causation of this condition has as yet been made. R. G. Freeman[6] suggests that the condition of the intestinal contents interferes with the absorption of nutriment, which fact in turn accounts for the cessation of growth. It may be noted that Geeepointed out that children suffering from celiac disease do not grow during the periods when this disease is active.

Alexander Spingarn.

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Cell.—A cell is one of the elementary forms of organized substances of animals and plants. It is irreducible into more simple parts except by mechanical or chemical means; it is therefore the *histological unit*.

In recent years the belief has arisen that the cell is not the ultimate living unit of the animal or vegetable organism, but that the protoplasm and nucleus consist of ultramicroscopic granules, apart from the visible granules, representing groups of molecules. These are the *micella* of Nägeli, the *biophores* of Weismann, and the *biogens* of Verworn (1908). These seem to fulfil all the functions of the bioplasm and have specific characters in different cells. Those biophores or groups of biophores that constitute the nuclear chromatin of the germ cells are assumed by Weismann to include the representatives of all the specific biophores of the somatic cells and so represent transmitters of hereditary qualities.

Historical.—It is to the botanists that the credit of the discovery of the minute structure of living matter is due. At the end of the seventeenth century Malpighi and Grew demonstrated the fact, although Leeuwenhoek anticipated the same in published drawings, that plant tissue was made up of small spaces with firm walls, and that these spaces were filled with fluid. They called these spaces cells, from the Latin "cella," a little cavity or space. Further investigation showed Fontana that this plant cell contained, in addition to the fluid, a somewhat granular substance and that this granular mass contained a darker spot, which spot we now know to be the nucleus. It was R. Brown (1831) who recognized the nucleus to be an integral portion of the cell.

Investigation of animal tissue by Schwann, Purkinje, Valentin, Müller, and Henle (1830–40) showed that it was composed of elements similar to those of plant tissue. In 1838 Schwann, as the result of his investigations, announced the fact that animal and plant tissues were made up of similar elements, and he defined these elements, the cells, as "small vesicles, with firm walls, enclosing fluid contents." It was Schwann who advanced the idea that the cell was the basic unit of higher animal organisms and this "cell theory" still maintains.

As the investigation of the plant cell continued, it was found that in many instances it was completely filled by this granular substance. Purkinje, in 1840, called this *protoplasm*, but this term did not come into general use until von Mohl applied it, in 1846.

to the living substance of plant cells. The same substance had been described by Dujardin in the Infusorians as "sarcode" and it was soon recognized that these two substances possessed the same properties.

Up to this time the cell wall was considered an essential structure and when masses of protoplasm without cell walls were found, although identical in protoplasmic structure with the accepted cell, they were called protoplasmic bodies by Remak. It became soon recognized by Leydig (1856) and emphasized by M. Schultz (1860) that the cell wall was frequently absent and hence not an essential structure. This paved the way for Leydig's definition of a cell—"a mass of protoplasm furnished with a nucleus"—that still holds to-day. This definition, however, is not absolute as certain cells of the human body (red blood cells and platelets) possess no nucleus. In addition, as pointed out by Dobell (1909) many protozoans and phytozoans possess no nucleus but particles of a basichromatic nature, called *chromidia* that take the place of the nucleus.

Structure of the Cell.—A great deal has been learned with regard to the structure of the cell within the last decade. These discoveries will be considered in the discussion of the structure of a cell. The parts of a typical cell (Fig. 1270) are as follows:

1. Cytoplasm { *a*. Spongioplasm. *b*. Hyaloplasm.
2. Nucleus { *a*. Chromatin. *b*. Achromatin.
3. Centrosome.
4. Nucleolus.
5. Cell wall.

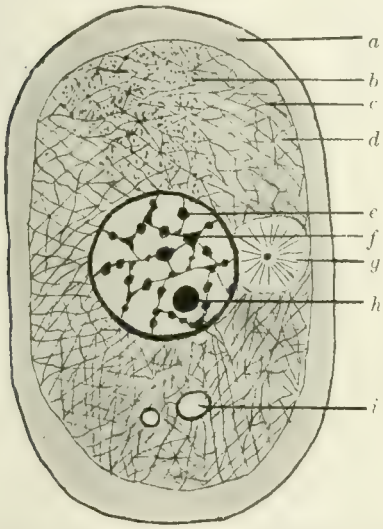

Fig. 1270.—Diagram of a Cell. *a*, exoplasm; *b*, microsomes; *c*, spongioplasm; *d*, hyaloplasm; *e*, chromatin; *f*, karyosome; *g*, centrosome; *h*, nucleolus; *i*, vacuole.

1. The *cytoplasm* (*cell body*, *protoplasm*) is a rather viscid substance, usually neutral in reaction and composed of (*a*) water that comprises about two-thirds of the weight; (*b*) inorganic substances as compounds of calcium, potassium, sodium, and chlorine, phosphorus and oxygen, the latter free or in combination; (*c*) organic salts, usually of phosphorus and iron in the form of proteins and nucleoproteins. In addition, certain nonprotein substances as lecithin and cholesterin are essential components of protoplasm.

Living protoplasm, as in *Ameba limax*, even under the highest magnification shows no apparent structure, while in other cells a reticular structure may be seen. This reticular structure is brought out clearly in all cells by the use of fixing agents. At present there are two theories in regard to the structure of protoplasm, the *reticular* which is supported by most of the investigators and the *honeycomb* or *foam* structure as advocated by Bütschli and his followers. Bütschli maintained that this reticular structure really represented a honeycomb and that the network was an illusion.

Following the reticular theory, the *cytoplasm* consists of two main portions, the network called the *spongioplasm* or *cytoreticulum* (Fig. 1270) and the *hyaloplasm* or *cytolymph*, that fills the interstices. These vary in proportion in the different cells. In young cells the hyaloplasm predominates, but as the cells grow, the spongioplasm increases while the hyaloplasm relatively decreases. In the hyaloplasm and at the nodal points of the reticulum are seen small bodies called *microsomes*, that tend to give the protoplasm a granular appearance. These bodies are usually absent near the periphery of the cell and that area constitutes the *ectoplasm*.

In the highly specialized nerve and muscle cells a greater fibrillar differentiation is noted so that the ordinary appearance of protoplasm is hidden. These fibrils are also constant structures in glandular and ciliated cells, though in a lesser degree. Fibrillation is also noted as a transitory character in dividing cells.

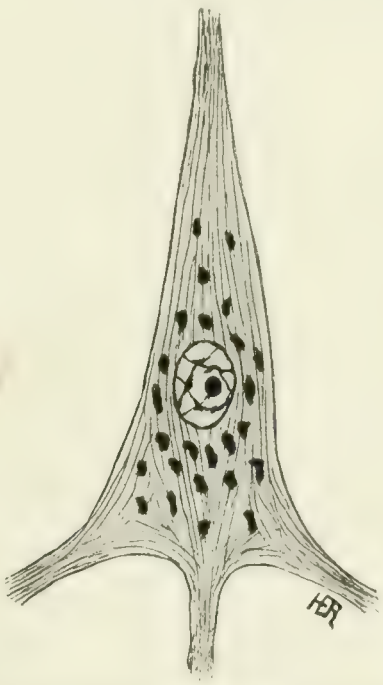

Fig. 1271.—Nerve Cell Showing Corpuscles of Nissl and Fibrils (Mitochondria) in the Protoplasm.

In the hyaloplasm other structures besides microsomes are seen. These may be (1) *granules*, as seen in gland cells, leucocytes, and the nerve cells (Nissl's corpuscles); certain other granules seem to be connected with the formation of contractile fibrils and other active portions of the cell protoplasm and have been, therefore, called *mitochondria*. (Fig. 1271.) Sometimes these fibrils thus formed collect into a spherical mass near the nucleus and then receive the name of *paranucleus* or *chondromitome*. Mitochondria have been carefully investigated in the past five years. In animal cells they have been studied especially by Meves (1909), Duesberg (1910) and in plant cells by Lewitzky (1911), Rudolp and Guilliermond (1912). Maximow (1913) studied these granules in living

plant cells and corroborated the works of others upon fixed tissues. These granules seem related to metabolic activities of the cell, to the formation of fibrillæ in muscle tissue, and in plant cells to the formation of the trophoplasts and chloroplasts. (2) Fat globules occur in the hyaloplasm of some cells; (3) vacuoles, clear areas of variable size; (4) pigment; (5) glycogen; (6) crystals and crystalloids.

Canaliculi in the cytoplasm were first noted in nerve cells by Golgi (1898) and in glandular cells by Negri (1900) and in epithelium by Holmgren (1902). Since then they have been demonstrated in many cells. Holmgren believed these to be permanent channels in the cell protoplasm, while von Bergen insists that they are transitory.

The protoplasm responds to certain stains as eosin, carmine, and the acid aniline dyes, called *protoplasmic* stains.

In 1892 Bütschli published the results of his observations on the minute structure of cytoplasm. He claimed that the reticular appearance was due to the fact that it was a *foam* or *emulsion*, being made up of numerous microscopic vacuoles, the walls of which were in close apposition, so that the microscope showed them only in optical section and not their surfaces. In order to confirm this theory he made numerous experiments and finally succeeded in producing what he called "artificial cytoplasm," which when viewed with the microscope had nearly the same appearance as the spongioplasm of a cell. This artificial cytoplasm was made by rubbing up olive oil with cane sugar or potassium hydrate. A drop of this mixture was placed on a slide, a small drop of water was added, and the whole was covered with a cover glass, the weight of which spread it out in a thin layer. From these experiments he concluded that cytoplasm was a mixture of fluids of different densities, the heavier forming the walls of the vacuoles, while the lighter collected in their cavities.

2. The *nucleus* (Fig. 1270) is usually a sharply outlined portion and conforms in general to the shape of the cell. It is usually completely surrounded by the cytoplasm, but in some cells it projects beyond the surface. It seems to preside over the nutritive and functional activities of the cell and plays an important part in cell division. Its structure resembles somewhat that of the protoplasm in that it consists of a network, the *chromatin* within which is found the nonfluid portion, the *achromatin* or *karyoplasm*. In addition, there is a distinct limiting membrane, the *nuclear membrane*.

The chromatin in a resting nucleus forms an irregular meshwork. In reality it consists of the real chromatin in the form of more or less irregular granules strung upon a delicate thread called the *linin* thread. These chromatin granules consist of nuclein containing a variable quantity of nucleic acid in combination, and respond to certain basichromatic stains. The depth of the stain depends upon the amount of nucleic acid. The linin threads, on the other hand, respond to the oxychromatic stains and may show contractility.

At nodal intervals larger masses of the chromatin may be seen and these structures are called *karyosomes*. During cell division these chromatin granules form a certain definite number of individual masses called *chromosomes*. According to Rabl the chromosomes may, apparently but not in reality, lose their identity. In fact, Boveri and O. Hertwig have pointed out that in some nuclei with few chromosomes this condition can readily be seen. The achromatin or karyoplasm resembles the hyaloplasm in appearance and affinity for stains and responds to the oxychromatic stains. It is clear and structureless in appearance in the living state. During cell division the karyoplasm mingles with the hyaloplasm. The *nuclear membrane* in resting cells is a solid unbroken membrane, though in rare cases it may be perforated. It consists of *amphipyrenin* that responds to the basichromatic dyes. The chromatic network takes origin from its inner surface and forms a meshwork, the spaces of which may be irregular or regular in size.

The nucleus conforms somewhat to the cell in shape, so it may be oval, spherical, rod-like, spindle-shaped, or lobulated as in some leucocytes. Although usually much smaller than the cell body, it may occupy almost the entire cell, as in the small lymphocytes and the granule cells of the cerebellum. The nucleus may be absent as in normal red-blood cells and respiratory epithelium and surface cells of the epidermis, but these all at one time possessed a nucleus. Usually but one nucleus exists in each cell; exceptions are liver cells, heart muscle, and leucocytes, where two or three may be found, and voluntary striated muscle where hundreds are found in each cell or fiber.

3. The *centrosome* (Fig. 1270) is a small area found near the center of the cell, but usually outside of the nucleus. It has not been demonstrated in all cells. Perhaps this is due to its exceedingly small size and the difficulty of the stain technique. It was first noted by Flemming and Kupffer in 1875, but its significance was not realized until 1887 through the work of Boveri and von Beneden. It consists of a small centrally placed body, the *centriole* surrounded by a clear area from which radiate a large number of delicate threads, apparently linin. This clear area is called the *attraction sphere* or *centrosome*. (This term has often been restricted to the centriole). Occasionally the centrosome is double (*diplosome*); in cells with several nuclei or a lobulate nucleus the centrioles may be numerous; again in ciliated cells small nodules are seen at the bases of the cilia and these are probably multiple centrioles.

The centrosome presides over cell division, initiating this process by its own divisions. In the resting cell it seems to preside over the motion of the whole cell as in pigmented cells and leucocytes; in ciliated and flagellated cells, it presides over the action of these processes. The centrosome responds to Heidenhain's iron hematoxylin stain.

4. The *nucleolus*, or *plasmosome* (Fig. 1270) is a body of variable size found free in the karyoplasm of the nucleus. It is usually structureless, but may present vacuoles or stain differently in parts. It is sometimes confused with the karyosome above mentioned. It may be absent or several may be present. The function of this body is not understood. Some observers claim that the nucleolus assists in the formation of the central spindle during mitosis; others, Montgomery (1898), claimed that they are products of degeneration and Walker (1908) showed that the nucleolus, either as a whole or in part, may be extruded into the protoplasm and thereby furnish materials that become further changed into secretion granules or other products of cellular activity.

5. The *cell-membrane* is no longer considered an essential portion of the cell. When present it represents the results of the activity of the cell. It is formed by secretion or is derived by the alteration of the ectoplasmic portion of the cell. The ovum exhibits the best example of a cell wall. Those cells that possess no membrane are limited by a delicate film composed probably of lipoids (cholesterin and lecithin) that is physically and probably chemically different from the rest of the protoplasm.

Cells in the human body vary greatly in size and shape. The smallest are the granule cells of the cerebellum and cerebrum and the small lymphocytes (4μ*), unless we classify the blood platelets as cells (1μ to 2μ); the largest individual cells are the large nerve cells and giant cells of the bone and marrow (80μ). The largest cell is the ovum (220μ to 320μ).

*A micron (μ) the unit of microscopic measurement is the $\frac{1}{1000}$ part of a millimeter, or $\frac{1}{25000}$ part of an inch.

Vital Properties of Cells.—Under this heading are grouped the phenomena of *movement*, *irritability*, *metabolism*, and *reproduction*.

Cells exhibit the phenomena of movement under three forms: *protoplasmic*, *ameboid*, and *ciliary*.

Protoplasmic movement is difficult of observation on account of the slowness of the process. It has been demonstrated in a few animal cells, and in plant cells it is easily observed, the streaming of the cytoplasm being an example. All animal cells are believed to possess it to a greater or lesser degree. It is made manifest by the changes in the form of the cytoplasm, by the movements of the microsomes, and by the changes in the position of the nucleus.

Ameboid movement is similar to that exhibited by the unicellular organism, the ameba. This phenomenon was described first by Rosenhof, in 1755, in the "proteus animalcule." Nearly all animal cells

Fig. 1272.—Ameboid Movement. (After Verworn.)

possess it to some extent, it being well marked in a special few, viz., the leucocytes, lymph cells, and wandering connective-tissue cells. If a living leucocyte be studied under the microscope, it will be seen to change continually its form (Fig. 1272). Gradually a bud-like mass of the cytoplasm will push out from some point, or several may start from different points. These *pseudopodia* may retract, or one may be extended for a considerable distance, the remainder of the cytoplasm flowing into it. Other pseudopodia are given off and the above process is repeated. These processes may be either massive or *lobed*, or fine and *spine-like*. By this means the cell will gradually crawl through the field of the microscope. It is by means of this ameboid movement that the leucocytes pass through the walls of the capillaries (diapedesis) and wander through the spaces of the tissues and organs or between other cells. This phenomenon is also exhibited when an ameboid cell takes in foreign particles, *i.e.* ingestion of food, or when phagocytes attack bacteria or tissues.

Ciliary movement is the power possessed by the hair-like appendages of certain cells (see *Epithelium*).

Irritability is the property that cells have of responding to external stimuli. This property is exhibited best in unicellular forms and others that possess no nerve system; in these it is a primary change in the cell. These stimuli, though almost innumerable, may, in a general manner, be grouped as mechanical, electrical, and chemical in their nature, or as due to heat and light.

All cells do not react in the same manner to the same stimulus, nor do all stimuli cause the same reaction in an individual cell. The response of a cell to a specific stimulus depends upon its structure. Some, those of the organs of vision, for example, respond to light only; while others may respond to one or more stimuli.

Under *mechanical stimuli* are classed pressure, violent shaking, and crushing, any one of which causes cells to react in some manner.

While *heat* is a necessary condition for the vital activity of cells, it must be confined within rather fixed limits; these varying considerably, however, for different cells. If the temperature be raised to 40° C. (104° F.) the vitality of the cell is destroyed, but, on the other hand, the temperature may be lowered to a considerable extent without the cell being killed. An increase of heat above that at which a cell normally exists causes a marked increase in its vital processes, until the heat-rigor point (40° C.) is reached, when a coagulation takes place and the cell is killed. Lowering of the temperature below the normal produces a gradual diminution of activity until the cold-rigor (0° C.) point is reached, when the cell passes into a "narcotic" state. Apparently cells can remain in this state for a considerable length of time without their vitality being destroyed, for if they be gradually warmed up to their normal temperature their vital functions are resumed.

Light, in the higher order of animals, is believed to be a stimulus to the cells of the organs of vision only. In some of the lower animals, other tissue cells, especially those of the skin, respond to its stimulation.

Electrical stimuli, when applied in the form of weak currents, cause an increase, strong currents a decrease, in cell activity. If the latter are continued for a considerable length of time they cause the death of the cell.

Chemical stimuli are almost numberless and at present their manner of action is not thoroughly understood. Some cause contraction, some increased movement, others increased secretive activity, etc. A striking example of the unilateral action of chemical stimuli is that known as *chemotaxis*. This is the property possessed by certain cells of responding to the stimulation of chemical substances introduced into or formed in the body. Some substances cause the cells to approach them—*positive chemotaxis;* others repel them—*negative chemotaxis*. The leucocytes respond quickly to this form of stimulation. Such movements may be produced by the addition or subtraction of water, producing relaxation and contraction, respectively. Chemical action is also dependent upon the concentration of the salts and upon the contained electrodes. Chemotaxis plays an important rôle in many physiological phenomena, as for example, the tendency to seek oxygen, the attraction of leucocytes toward bacterial activity, and the attraction exerted by the ovum upon the spermatozöon.

Metabolism is the property which cells possess of absorbing and of giving off materials. The former process is termed constructive metabolism or *anabolism*, the latter destructive metabolism or *catabolism*. The anabolic products are retained in part by the cell for its nutrition and the remainder are given off as its specific secretion. Catabolic products are mostly thrown off as excretions.

Reproduction.—All of the multitude of cells entering into the formation of the various tissues and organs of the adult animal body are derived from one original cell, the fertilized ovum that represents the union of male and female elements. Every cell is the result of the division of a preexisting cell (mother cell) into two cells (daughter cells). This process is known as *cell division*.

Two chief forms of cell division are now recognized: indirect cell division (*karyokinesis*, *karyomitosis*, or *mitosis*) and direct cell division (*amitosis*).

Indirect cell division, or *mitosis*, is the process by which the vast majority of the cells of the animal

body divide. In this form of division the intranuclear network undergoes a series of complicated changes; the nucleus divides, and finally the cell body itself separates into two equal portions.

The process is divided into four stages: the first stage, *prophases*, in which the nucleus undergoes a series of preparatory changes; the second stage, *metaphases*, in which the division and separation of chromosomes takes place; the third stage, *anaphases*, in which the chromatic material is distributed to each pole and the cytoplasm begins to divide; finally the fourth stage, *telophases*, in which the complete division of the cell occurs with the formation of resting nuclei in the daughter cells.

Prophases.—This stage is initiated by the division of the centrosome which occurs before visible changes appear in the nucleus. This body, which usually

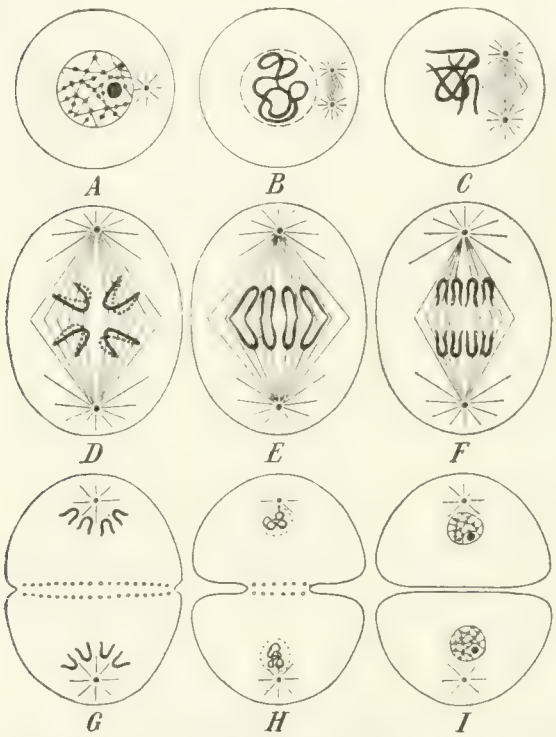

FIG. 1273.—Diagram of Mitosis. *A*, resting cell; *B*, beginning prophases, nuclear membrane disappearing, nucleolus gone, chromatin forming spirem, centrosome divided; *C*, chromosomes formed, centrosomes migrating; *D*, equatorial plate and splitting of chromosomes, end of prophases; *E*, metaphases, separation of daughter chomosomes with formation of nuclear spindle; *F*, complete separation and migration of daughter chromosomes, end of metaphases; *G*, anaphases, chromosomes near respective centrosomes, protoplasm shows constriction; *H*, diasters with continued division of protoplasm; *I*, telophase, complete division of the cell, each daughter cell in resting stage.

lies outside of the nucleus, divides and each part surrounded by its attraction sphere migrates toward the opposite pole of the cell. Between the two separating centrosomes a delicate spindle composed of linin threads, the *central*, or *achromatic spindle*, is noted. This shows best (Fig. 1273, *D*) after the nuclear changes have been completed. In the meantime the chromatin granules of the nucleus run together to form a thin, smooth, closely convoluted thread, *spirem* (*B*), while the nuclear membrane and nucleolus disappear and the achromatin mingles with the hyaloplasm. The spirem ultimately breaks up into a definite number of segments called *chromosomes* (*C*), that are U-shaped and arrange themselves around the equator of the cell with closed ends directed toward the center. The figure thus formed is called *monaster*, or *equatorial plate* (*D*), and represents the end of the prophases.

The number of chromosomes is definite for each species and in forms that arise from sexual reproduction the number is always even. In man the number is twenty-four.

Metaphases.—During this stage the chromosomes split longitudinally, this division starting at the closed end; the segments begin to separate, one-half being directed toward each centrosome forming thus a second, or *chromatic spindle* (*E*), within the central spindle. Some observers believe that this separation is due to the traction exerted by some of the central spindle fibers that are said to be attached to the chromosomes. The daughter chromosomes move apart (*E*, *F*, *G*) toward their respective centrosomes constituting *diasters*.

The Anaphases.—During this stage the diasters are in the immediate neighborhood of the centrosomes and the chromosomes now unite and send out lateral twigs. The cytoplasm at the equator (*H*), shows a double row of granules and a peripheral constriction indicating the division of the cell body.

The Telophases.—During this stage the cell becomes completely divided. The nuclear membrane and nucleolus reappear and the chromatin assumes the appearance of a resting nucleus. The centrosome likewise changes to that of the resting stage and division is completed (*I*).

Direct Cell Division or Amitosis.—This form of cell division was formerly thought to be the usual form, but is now known to be restricted to some cells of the bladder, cells of Sertoli of the testicle, and giant cells

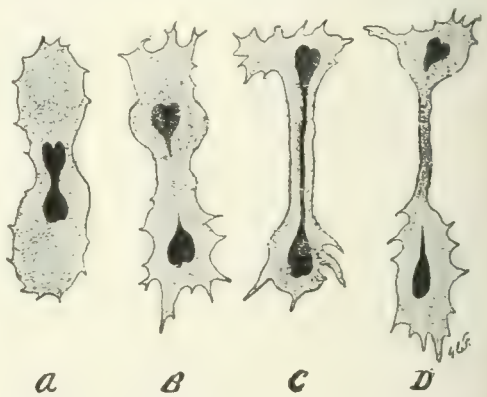

FIG. 1274.—Direct Cell Division or Amitosis. (After Arnold.) *A*, constriction of the nucleus; *B*, complete division of the nucleus, commencing constriction of the cell body; *C*, daughter nuclei still connected by a thread of nuclear material; *D*, daughter cells still connected by a narrow band of cytoplasm.

of the bone-marrow, and occasionally to leucocytes and gland cells. By some it is considered a sign of degeneration. The nucleus in this form of cell division divides without the intranuclear network undergoing the same complicated changes as in the indirect form.

The nucleus first becomes constricted (Fig. 1274, *A*); this constriction gradually increases and finally cuts the nucleus into two parts, forming daughter nuclei; these daughter nuclei draw away from each other by ameboid movement (Fig. 1274, *B*). At times the complete division is delayed and the nuclei remain connected, for some time, by a narrow thread of the nuclear material (Fig. 1274, *C*). Division of the cytoplasm takes place by the development, at first, of a constriction between the nuclei, and then finally by the entire separation of the daughter cells thus formed. Like the nucleus, the cytoplasm may in

some instances remain connected (Fig. 0005, *D*), or its division may be delayed while the nuclei go on dividing, the result being an accumulation of nuclei and the formation of multinucleated cells.

The innumerable cells found in the adult organism, though derived from a common parent, the ovum, lose in many respects all resemblance to that cell. They assume new forms and functions, these being brought about by a process of cell differentiation.

After the fertilization of the ovum it divides by mitosis and at first the daughter cells resemble the mother cells. Soon changes make their appearance in the cells and they can be grouped into two forms. These two forms continue to multiply and finally they become arranged into three distinct layers—*the layers of the blastoderm.* From these layers of the blastoderm (*ectoderm, mesoderm* and *entoderm*) all of the tissues of the body are derived, each layer furnishing certain specific tissues. H. E. Radasch.

Cellia.—A genus of mosquitos, family *Anophelinæ*, in which the body and palps are scaly, the abdomen being completely covered, and which have tufts of scale-like hairs on the head. See *Insects, poisonous.* A. S. P.

Cellulase is an enzyme found in the alimentary canal of certain herbivora capable of transforming cellulose into lower carbohydrates thus leading to the utilization of cellulose. F. P. U.

Cellulose.—$(C_6H_{10}O_5)$. This is the complex carbohydrate, or group of carbohydrates, which forms the chief constituent of the cell walls of plants. The true celluloses are mainly characterized by their great insolubility. By the action of concentrated sulphuric acid cellulose is converted into a substance called amyloid which gives a blue color with iodine. Nitric acid or a mixture of nitric acid and sulphuric acid changes cellulose into nitric acid esters, or nitrocelluloses, which are very explosive. When boiled with sulphuric acid cellulose may be transformed into dextrose. In man it is probable that cellulose is digested to a very limited extent only. See *Aliment.* Frank P. Underhill.

Celsus, Aulus Cornelius.—The time and place of birth of Celsus are not known, but there can be scarcely any doubt that he flourished during the reign of the Roman Emperor Augustus (circa 15 of the present era). By some he is spoken of as the Latin Hippocrates, by others as the Cicero of physicians. His principal work is entitled "De arte medica libri octo," but under the title of "Artium libri" he also wrote a veritable cyclopedia, in which each branch of science—agriculture, rhetoric, and perhaps also history, law, and the military art—is treated with such a degree of thoroughness that one finds it difficult to decide to which of these different branches of learning Celsus devoted himself chiefly. The writer of Celsus' biography in the *Dictionnaire Historique de la Médecine* expresses the belief that, notwithstanding the thorough knowledge which he possessed of medicine as a science, he never practised it as an art. However this may be, it is certain that his treatise on "The Art of Medicine" gives us the most perfect picture of this art, especially its surgical aspects, as practised in antiquity that we possess.

The earliest edition of "De arte medica" is that published at Florence, Italy, in 1478; of the later editions the number is almost unlimited. A. H. B.

Cenesthesia.—This term (also written cœnæsthesia) is fairly straight Greek for "common sensation;" it should be used to include all the sense-experience of the body save that arising through stimulation of the eyes, the ears, the taste-cells, and the smell-cells. Woven together in the way so well emphasized by several recent researches (no one kind of sense-organ ever being stimulated singly under original natural conditions), the cenesthetic sensations constitute the *sense-fabric* which in turn makes up in a way the warp and woof of consciousness and of the effective subconsciousness.

Cenesthesia, then, includes the sensations arising in the viscera (especially such of them as are hollow), in the bones, the tendons, the muscles, the joints, and the skin. The proper distribution of the dozen or so different forms of cenesthetic sense-organs which have thus far been described by the histologists has not yet been worked out, so that it is still inexpedient to try to assign definite functions to definite receptors. It cannot be too strongly insisted, however, that functionally cenesthesia is always a most complex compound experience produced by the probable central fusion of many thousands of sense-organs of many different kinds in the viscera, skin, and action-system (muscle, joints, tendons, bones), the stimulus of these being various modes of mechanical (or thermic) energy in the body and outside of it, coming mostly from the *universal inherent movement* of the organism. Each feeling and emotion and motive differs from every other, for example, because its own particular phase of the cenesthesia is unique, each phase corresponding to an unique group of bodily movements or strains or innervations at least.

There are three very general principles of relation between the common sensation and the movement of the body: (1) the sensations are increased when the movements "begin" after resting; (2) when the movements are increased; and (3) when the receptor surfaces are deranged, for example, by inflammation.

Henry Head of London has worked out what he considers to be constant dermal zones of pain-experience, related to disturbances within the thoracic and abdominal cavities; these demonstrate his useful principles of "referred pain." The ganglion on the posterior spinal root probably serves to connect (through the "basket" reticulum) the sensory sympathetic with the afferent spinal pathways proper. We need more information about sympathetic sensation.

The sensations of heat and of cold are important phases of the experiences stimulated in the skin, but we know relatively little as yet concerning their relations to each other or to pressure and pain, except that they occur naturally more or less together. The atmospheric influences, for example, affect the skin and each kind of receptor in it all at once; herein in some way lies a part at least of the tremendous advantages of the open, especially of moving open air (Sewall). Here is the key to the important ventilation-problem, especially in schools. (See an article by the present writer on "Certain Physiologic Aspects of School Hygiene," in *Education*, xxxi., 1, September, 1910.)

Each organ and tissue of the body has receptive fields of its own and each contributes in its own way to the total cenesthesia. It need not be emphasized, so obvious is it, that until these partial cenesthesias, so to say, are better known and neurologically more fully understood, we cannot expect really to understand either the subjective symptoms of disease and dysphoria or the details of the feelings, emotions, and motor ideas which determine behavior.

Among the varieties of cenesthic feelings from the special organs the following may be mentioned, for each organ has a sensation-complex of its own.

Head.—Sensations arising from numerous vasomotor blood-pressure changes. Feelings of fullness or of emptiness; pains, aches, etc., of many types

and locations. Muscular strains which are often indistinguishable subjectively from the inside experiences. The eye muscles and the ear muscles give rise to complex kinesthesia. It is a debatable subject still whether the brain itself gives any feelings or sensations, such, for example, as the feeling of effort so much discussed in the nineties by James and Ladd. Electrical influences exert themselves, for some people can tell when a thunder storm is coming. There are distinct feelings of general fatigue in the brain, after strenuous shopping, fairs, etc., especially. There are also many sensations that arise in the neck (mostly vascular) and in the upper part of the spine.

Lungs.—The nasal fossæ, the larynx, the bronchi, etc., give many sensations; the perfection of the ventilation of the lungs normally determines whether respiration is a pleasant or unpleasant experience. The respiratory muscles, and the pleuræ when inflamed, give rise to all sorts of pain, but possibly the muscular movements of respiration year in, year out, give more pleasure during life than any other one thing in the world! We are continually inspiring air, and if it be abundant and pure, there is distinct although slight pleasure with each breath. The descent of the diaphragm displaces more or less all the abdominal viscera, and thus gives rise to a very massive cenesthetic sensation, inasmuch as everything in the abdomen down to the coccyx is put under strain; they all have cenesthetic sensations in them. Respiration is thus the occasion of the most massive of all the experience coming usually from bodily movement.

Heart.—Rabbits and various other animals have separate depressor afferent nerves arising in the heart. Man has, however, various sensations going up the vagus nerve such as, for example, are often experienced from excessive smoking. The heart is affected by its efforts to shorten and lengthen in its vasomotor reactions. Angina pectoris gives rise to great agony. Terror, etc., may occasion decided feelings in the heart, whether palpitation or irregular action or even momentary stopping be the cause.

Alimentary Canal.—This has large groups of very various, numerous, and basal sensations. So have the glands in connection with it. Nervous dyspepsia merges into neurasthenia itself, and their cenesthesias are beyond description. Motor sensation and secretory sensations both are concerned with the functions of the alimentary canal, and others are connected with excretion or with the lack of secretion. Borborygmi are caused by hydraulic and other conditions in the gut and are felt as well as heard. The rectum has a large complex of sensations of its own. The tonus of the rectal sphincters gives rise to subconscious or conscious sensation. The ileocecal valve has sensations attached to its functions at times. The intestine has all sorts of sensations (neuritis, neuralgia, etc.) arising in obscure irritations and other defects.

The emotions are most intimately connected with the alimentary canal. One of the chief "seats" of the meotions is in this extensive portion of the vegetative apparatus. In hysterical and insane conditions, and in hypochondria, there is no imaginable limit to the influence of the gut and its "sensory" nerves on the mind of the sufferer.

Urinary Bladder.—This organ has a set of emotions of its own, and is a very sensitive viscus, especially to emotional tones. It has a rhythmic beat, like the other smooth-muscle viscera, and a considerable mass of sensations rises from it. As it begins to be overdistended it becomes more and more conscious The urethra has a set of feelings of its own. The tonus of the sphincters is an element in the subconsciousness.

Reproductive Apparatus—The generative mechanism has a very important and rich set of sensations of hundreds of kinds. (See Stanley Hall; "Adolescence.") The cenesthesia arising in these organs altogether forms a very important part of the "mass" of the subconscious, especially in adolescence. Compare the psychoanalytic work of Freud and his followers.

Spleen.—This viscus has a large amount of smooth muscle, and doubtless has a set of neural influences of its own.

Liver, Gall-bladder.—These, especially the latter, contribute to the cenesthesia.

Internally secreting glands (the thyroid, etc.) may have subconscious influence over the sensation-fabric that underlies consciousness, for they contain both nerves and smooth muscle.

Serous Membranes.—These are more or less well supplied with nerves and when inflamed give rise to sensations always apparently verging on pain and often painful in the most acute degree.

The considerable part taken by kinesthesia (including touch) and by the dermal experiences of heat and of cold in cenesthesia need not be rehearsed, but it must be remembered that they (especially the former) predominate as factors in cenesthesia.

H. Beaunis gives the best classification of the sensory modalities known to the writer in his "Les Sensations Internes," 1889.

Hysteria shows a richness of cenesthetic experience not approached in the normality of the mind. The reader is referred to the article on that interesting condition.

Paranoia likewise illustrates very strikingly to how large an extent the freer processes of mind (imagination, fancy, conception, perception, understanding, reason itself) depend upon and are colored or even determined by these largely subconscious nerve influences pouring eternally into the gray fabric of the brain.

Hypochondria is essentially a bad habit of overattention to cenesthesia especially in its visceral phases. These, of course, are best left to themselves as part of the reflex vegetative psychophysiological mechanism. GEORGE V. N. DEARBORN.

Centaurium.—*Centaury, Lesser Centaury.* The dried plant of *Erythræa centaurium* (L.) Pers. (Fam. *Gentianaceæ*). (N. F.)

This drug is a favorite simple bitter in Europe, where it is official in most Pharmacopœias. It is frequently imported for use in the United States. It is a slender herb, about a foot high, with erect branches. The leaves of the basal rosette are usually wanting in the drug. Those of the stem are mostly one to two inches long, sessile, oblong, obtuse, entire. The flowers are cymosely arranged and sessile, about one-half inch long, bright rose-purple, four- or five-merous. The narrow calyx-lobes are keeled, and about the length of the corolla-lobes, which are only about half the length of the corolla-tube. The four or five stamens have elongated anthers which twist as they become old. It usually occurs in commerce cut into short lengths. It contains bitter principles similar to those of gentian and chirata, and the dose, as a simple bitter, is the same, namely gr. xv (1.0.) H. H. RUSBY.

Centipedes.—Animals belonging to the order *Chilopoda*, class *Myriapoda*, and phylum *Arthropoda*. The body is elongated, flattened, and segmented; with a pair of legs on each segment. These animals have a pair of poison fangs on the under side of the head, but their bite is seldom of a serious character. See *Insects, poisonous.* A. S. P.

Cephaleine.—See *Ipecac.*

Cephalin.—This substance, at present classed with the lecithin group, is a monoamino-phosphatide whose formula is probably $C_{42}H_{82}NPO_{13}$. This com-

pound is widely distributed throughout the animal and vegetable kingdoms being especially abundant in the yolk of egg, testicle, muscle, kidney, and brain. On cleavage of cephalin it yields products of such a nature that its composition has been suggested to be dioxystearyl monomethyl lecithin. It is a substance which, although insoluble in, swells up in water. It is soluble in ether, glacial acetic acid, and chloroform, but is insoluble in acetone and in alcohol, either cold or warm. FRANK P. UNDERHILL.

Cephalhematoma.—*Definition.*—An effusion of blood upon or within the crania of newly born infants.

VARIETIES.—*Subaponeurotic,* the simplest, but uncommon—a bloody effusion immediately underneath the cranial muscles.

Subpericranial, situated between the pericranium and cranial bone—the most common.

Diploic, situated within the diploë—a rare form, and differing from others in that it continues to bleed when laid open. (This is explained by the abundant supply of arteries and veins in the reticulated structure of the diploë.)

Subcranial, generally situated between the skull and dura mater, and sometimes in the cavity of the arachnoid. A case of triple cephalhematoma is reported by Oui; it appeared after an easy spontaneous accouchement; spontaneous suppuration and opening of the occipital tumor; puncture of the left parietal tumor (the larger one of the two parietal tumors), followed by rapid recovery; non-intervention with the right parietal tumor, which very slowly underwent resolution.

PATHOLOGICAL ANATOMY.—The scalp generally retains its natural aspect. Exceptionally it becomes red and livid. Its substance remains uninjured, and the pericranium preserves its transparency. The effused blood is contained in a sac of fine membrane, having all the characteristics of condensed cellular tissue. It rests on the bone, from which it can be eaisily detached and underneath the pericranium, to whch it adheres, more firmly. Points of ossification can be observed on the under surface of this membrane. The earlier writers thought that the outer table of the skull was necrosed, carious, and destroyed, and that the ruptured vessels of the diploë gave rise to the hemorrhage. A bony ring forms in the majority of cases. It begins as soon as the separation of the pericranium is arrested, which is about the second day. This has been said to be only a delusion of the sense of touch, but its presence has been demonstrated by numerous autopsies. It is not, however, always present, being absent in tumors situated near a suture. There are many theories as to its causation. The following, by Virchow, is probably not only the most beautiful, but also the most plausible: The healthy cranium grows by proliferation of the inner layers of the periosteum. If, then, the pericranium, through the blood which is poured out, is held apart from the cranium, the bone-forming layers of the periosteum being still thrown off, they cannot reach that part of the bone for which they are intended, on account of the presence of the blood. Eager, however, to fulfil their office, they join themselves to the bone at the border of the tumor where the bone is still attached. Bland Sutton reports a case which had occurred in a monkey. Autopsy showed the bony ring. Similar formations of bone are observed in rabbits subjected to experimental elevation of the pericranium.

ETIOLOGY.—The etiology has occasioned much discussion. The reception of some injury by the child during parturition was long thought to be the cause. A number of observers failed to note that it succeeded difficult labors. The tumor occurred on parts not liable to pressure. Cases are reported after breech presentations, after cesarean section, and after painless labor, and it has been observed that a narrow pelvis in the mother is an infrequent accompaniment. It occurs in premature births. These tumors form on children of advanced age and on adults; sixty-six and two-thirds per cent. of the cases are males. While it is very easy to imagine how pressure during parturition might cause the tumors, yet it is very evident that in a large proportion this is not the cause but that it must be some fault of the blood-vessels. Intracranial hemorrhage is in reality a form of apoplexy and it is quite probable that the tendency is inherited. One case is on record in which the same mother gave birth to three children successively who had cephalhematoma. In a case reported by the author, the mother said: "Three of my other children died of convulsions, and I gave this one up as soon as they came on." These other children, too, might have had cephalhematomas, and there might have been an inherited tendency; or an unusual friability or thinness of the vessels, or incomplete development of the outer layer of the skull, might have been the cause. If cephalhematomas are caused by pressure in breech presentations, this must be due to the action of the cervix on the cord or neck of the child. Pressure during delivery undoubtedly has something to do with the causation of a considerable number of these tumors, yet there are many others which must result from a diseased condition of the blood-vessels, inherited or acquired. Heydecker reports a case which was due, in his opinion, to imperfect ossification of the cranial bones.

FREQUENCY.—The average, so far as it can be learned from the statements of authors, is 1 in every 235 children born.

LOCATION.—It is most frequently situated on the right parietal bone, then on the left, occasionally on the frontal, more rarely on the occipital and in the temporal regions.

DIAGNOSIS.—It is a disease of the newly born. Exceptions: One case has been reported in a child of six months, another in one of twelve months, a third in a man of twenty-six years, a fourth in one of thirty-six, and a fifth in a woman of forty-nine. These, however, are anomalies. One notices a tumefaction, usually one, two, or three days after birth. It develops gradually; it is of fluid character. It pulsates forcibly at the beginning, if connected with an artery; it loses this later, but fluctuation is always present. In size the tumor ranges from that of a hazelnut to that of a mass involving the whole surface of the parietal bone. The tumor is limited by the sutures in the three varieties situated between the pericranium and the dura mater; in the subaponeurotic and arachnoid varieties this is not so. The scalp is natural in appearance in the subaponeurotic variety. The bony ring is almost pathognomonic in the subpericranial variety, but is not so often present in those situated between the cranium and dura mater; in the other varieties it is absent. The diagnosis of internal cephalhematoma must be made from the symptoms of brain pressure, twitchings, convulsions, stupor, or paralysis which it may produce. The caput succedaneum occurs in the first twelve to thirty-six hours. Cephalhematoma is at birth either absent or scarcely noticeable, grows from day to day until, on the eight day, it attains its full size, and then, perhaps, the bony ring can be felt. The caput succedaneum pits on pressure, while the cephalhematoma does not. From hernia cerebri congenita it may be distinguished by the fact that this pulsates, while cephalhematoma simply fluctuates; hernia cerebri, furthermore, is not found on the parietal bones, but on the sutures and fontanels; it protrudes during the acts of coughing and crying, is partly reducible, and then causes slight convulsions. The

rim of bone resembles somewhat the elevated ring, but pressure of the finger on the tumor does not find a bony floor as in cephalhematoma. The skin over hernia cerebri is thin and hairless, in cephalhematoma it is normal. Fungus of the dura mater does not contain fluid, does not fluctuate nor feel doughy, has no bony ring, and the overlying skin is thick and blue. This form of tumor becomes smaller under pressure, and, besides, it seldom occurs in children. Atheroma and fatty tumors occur rarely at such a tender age. They can be differentiated by the trocar, but one must be careful to exclude hernia cerebri before using this instrument. There is no danger of confounding cephalhematoma with hydrocephalus externus, and the osseous circle will distinguish the former from aqueous cysts. Telangioma occupies the favorite seat of hematoma, but is not covered with hair, pulsates weakly, and is somewhat diminished in size by pressure.

Prognosis.—For the extracranial tumors the prognosis is good, for the intracranial it is bad. Death takes place mostly from exhaustion, brain pressure, and secondary hemorrhage; from rupture of the tumor; from necrosis or caries of the bone leading to perforation; from thrombosis of the cerebral sinus; from extension of the inflammation into the meninges and brain itself; from absorption of ichorous discharge, and from pyemia. Arthritis, phlebitis umbilicalis, pleuritis, scleroderma, intestinal hemorrhage, caries of the skull, and, in the internal variety, idiocy are among the results which may follow cephalhematoma.

Treatment.—Authors are divided; some follow the expectant, others the active plan. Some of those who use the knife wait till the eighth to twelfth day; a few make the incision earlier. The artificial evacuation of the blood is usually unnecessary, and may do harm; as a rule, non-interference is best. If pus forms it should be evacuated. Patton, in the case of his own son, aspirated on the twelfth day, removing twelve fluid drams of blood. The result was good and Patton recommends the operation highly. For the external varieties, warm aromatic fomentations, cold spirit lotions, pressure, and setons have all had their day. Treatment in intracranial cephalhematoma has not yet been attempted; but as the internal is almost always associated with the external variety, the latter being situated directly over the former, in the writer's opinion it would be advisable to trephine the skull to evacuate the tumor.

Edward Sydney McKee.

Cephalocele.—*Synonyms:* Encephalocele, Encephalocystocele, Hydrencephalocele, Cephalhydrocele, Meningocele, Hydromeningocele, Craniocele, Hernia seu Fungus seu Ectopia Cerebri. Hernia of the brain or meninges is a name given to a protru ion of a portion of the contents of the cranial cavity through an opening in the skull beneath the scalp. There is need of greater simplicity in what is now a rather confusing terminology, and it would seem that the best designation for all of these tumors as a class is cephalocele. There is a correspondence in application between this word and enterocele because of the similarity of their constituents. There is a hernial canal or opening in the skull, a hernial sac consisting of the dura mater, the hernial contents composed of whatever substance or fluid may be forced out from the cranial cavity, and finally the various coverings of the hernia, such as the pericranium, fascia, and skin. It is necessary, in a true cephalocele, that the dura mater form the hernial sac. The tumors formed beneath the scalp in traumatic esions of the skull and dura, by the pouring out of cerebrospinal fluid, are not true cephaloceles, and are more properly termed *pseudomeningoceles.* Protrusion of brain substance in compound fractures of the skull is not considered here, though sometimes improperly called a hernia cerebri; the correct designation is *prolapsus cerebri.*

The varieties of cephalocele depend upon the contents of the tumor. Hence we have a *meningocele* where the hernial contents are cerebrospinal fluid alone pressing out the dura mater; a *hydrocephalocele* where the tumor consists of an internal hydrocephalus expanding and forcing outward the ventricular walls; and, finally, an *encephalocele,* composed wholly of brain substance with more or less fluid usually surrounding it.

These tumors are mostly of congenital origin, but there are certain rare cases in which they are acquired after birth, through disease of the cranial bones or traumatism. It is usual, therefore, to distinguish two forms of cephalocele, the congenital and the acquired. In describing the latter it will be best to use the prefix *pseudo.*

Under this heading may also be included the *decompression cephalocele* following palliative operations for the relief of increased intracranial pressure; as in tumor and acquired internal hydrocephalus.

Congenital Cephalocele.—These tumors almost always have their peduncles at or in the immediate neighborhood of some cranial suture. The great majority are in the anteroposterior median line, as a rule either in the frontal or in the occipital region. Accord-

Fig. 1275.—Nasofrontal Cephalocele. (Pfandler u. Schlossmann, Handbuch der Kinderheilkunde, 1906.)

ing to Giovanni Reale, who collected 68 cases of cephalocele, 10 were at the nasal root, 9 in the frontal suture, 5 at the posterior fontanelle, and 22 in the occipital bone, the rest arising from some of the lateral sutures. Larger tabulated 85 cases, 44 of which were occipital, and 41 frontal or sincipital. The favorite location of the sincipital tumors is at the root of the nose, either at the inferior part of the frontal suture or at the junction of the ethmoid and frontal bones. (Fig 1.) The hernial canal or opening is generally bounded by the separated or more or less malformed ethmoid, frontal, nasal, or lacrymal bones, and sometimes even by the nasal process of the superior maxilla. Fenger,[1] in an article entitled "Basal Hernias of the Brain," describes such sincipital tumors as differ from the others in not protruding in the face. The least uncommon form is the sphenopharyngeal cephalocele, protruding into the nasal or nasopharyngeal cavity. These may be more common than is supposed. They may be mistaken for nasal polyps. The occipital cephaloceles

are the most frequent of all. They are situated either in or near the posterior fontanelle, or lower down under the occipital protuberance, where the hernial opening may be conjoined with the foramen magnum. Hernial protrusions from other sutures are much more rare, although they do occur in the greater fontanelle, in the squamous suture, or between the ethmoid and sphenoid bones at the base of the skull.

Cephalocele is uncommon, Trélat finding but 3 in 12,000 births, and Vines 1 in 5,000. It is said to be more common in females than in males, though Z. Lawrence, quoted by Erichsen,[2] collected 39 cases, 21 of which were in males.

Fig. 1276.—Occipital Cephalocele (Pfandler u. Schlossmann, Handbuch der Kinderheilkunde, 1906.)

The tumors vary in size from that of a pea to that of a child's head. The occipital are always the largest, and are usually hydrocephaloceles. The sincipital tumors are, as a rule, small and simple encephaloceles. Meningoceles may exist in either place, but are more common behind. Hydrocephaloceles are rarely sincipital, owing to the positions and conformations of the ventricles, which are more apt to dilate posteriorly.

The occipital *hydrocephaloceles* are usually constricted at their base, often pedunculated, almost globular in form, and seldom attached by broad bases. They generally contain the dropsical posterior horns of the lateral ventricles or their fetal analogues, when the defect is situated above the tentorium. Those in the lower occipital region enclose the cerebellum and the hydropic fourth ventricle. In some of the largest hydrocephaloceles have been found a great part of the cerebrum, the cerebellum, the fourth ventricle, and the quadrigeminal bodies. The protruding cephalic parts are commonly of inferior or defective development, often difficult to recognize as brain substance, owing to cystoid degeneration and sclerosis (Huebner). P. Berger[3] reports an extirpation of an encephalocele and a case by a colleague (Périer) in which both specimens were carefully examined by Ranvier and Suchard, showing features not hitherto described. In both were found histologically a mixture of nervous elements of both cerebrum and cerebellum without lines of demarcation, and Berger regarded these tumors as forming a variety of central neuromata such as have been described by Virchow (tumors formed in the ventricles of subjects afflicted with congenital hydrocephalus). Berger proposes the term *encephaloma* for this species of encephalocele. Sometimes the constriction at the hernial opening is so great that there is marked stasis of blood in the pia, which may lead even to extravasations. Occasionally these tumors present longitudinal constrictions caused by the venous plexus or by the falces of the dura. The quantity of fluid contents varies, but may reach two quarts. It has been found to be rich in albumin, with a specific gravity of 1.010–1.012.

The *meningoceles* of the occipital region are quite as large as the hydrocephaloceles, and similar in shape, while those of the sincipital and lateral areas of the skull are much smaller. One very large meningocele held fluid which had a specific gravity of 1.004, and contained a small quantity of albumin, uric acid, chloride of sodium, and biliary coloring matters (Heineke).

The *encephaloceles* are usually small tumors with broad bases, having a diameter as a rule between one and three centimeters, generally occupying a position at the root of the nose, and containing often, besides cerebral substance, a small quantity of subdural fluid.

Pathology.—There are several theories advanced to account for the origin of these congenital tumors. One is, that there is a limited ventricular dropsy, which by presssure at some certain circumscribed portion of the skull expands and separates the cranial bones and thus protrudes. From a hydrocephalocele thus formed an encephalocele may be produced later, by reabsorption of the dropsical fluid; or a meningocele, by a recession of the cerebral substance into the cranial cavity. The arguments against this hypothesis are, that there would scarcely be a circumscription of the dropsy as imagined, but rather a tendency to a general hydrocephalus; and, furthermore, Ackermann and Heineke have determined that there is a diminution, and not an increase, of intracranial pressure in cases of cephalocele.

A more probable theory as to the etiology of these tumors is, that they originate in the early embryological periods, when the cerebral vesicle and its fluid contents are in process of growth, and their osseous capsule is not yet developed. There is then an arrested or defective evolution of the cranial vault, as a result of which complete closure of the skull does not take place, and a circumscribed portion of the fetal brain vesicle protrudes. According to this hypothesis, hydrocephalocele would belong to an earlier stage of development, and encephalocele to a later, when the protruding portion of brain no longer exhibits the configuration of the fetal brain vesicle as it does in the former. In like manner, meningocele may originate either by the mere extrusion of the dura mater through pressure of the subdural fluid, or by the bursting of a hydrocephalocele, or it may be the remnant of a disorganized encephalocele. Meningocele might also spring from the cerebral vesicle in the earliest stages of development, as a mere membranous cyst without brain substance. Yet, if the defect in the skull were the only factor in the formation of these tumors, it would be difficult to understand why they are not present in every child in the open cranial spaces, the fontanelles. We are compelled, therefore, to recognize, as another factor in their causation, a general or partial hydrocephalus, either internal or external.

This conception of the embryological origin of cephaloceles is corroborated by the fact that most of them are found in front of and behind the head, in the median line, which is the most marked direction of growth of the cerebral vesicle; and that other defects and malformations of the skull, face, spine, feet, etc., are often observed in connection with these cases. Thus, striking departures from the normal shape of the skull are particularly noticeable in hydrocephalocele and the large meningoceles, where there is often asymmetry, thickening of the sutures, microcephalus, flattening from before backward, and sometimes hydrocephalus; while in the simpler tumors the skull presents, as a rule, a wholly normal configuration.

What may be the ultimate causes of these defects

can only be surmised. Premature union of the meninges with the amnion, and injuries to the fetal head *in utero*, may sometimes be the occasion of their development. Berger[3] reviews all the theories in detail (intracranial pressure from limited dropsy, arrest of fetal cranial development, fetal craniotabes) and believes himself that an encephalocele is a primitive protrusion of part of the brain previous to the formation of the cranial vault. He agrees with Fleischmann and Niemeyer that the cause of a simple encephalocele may lie in a hyperplasia of brain substance.

Lindfors[4] discusses at length the history, etiology, and surgical treatment of congenital cerebral hernias, bringing the whole subject well up the date of his

Fig. 1277.—An Irregular Tumor Proceeding from the Cranial Cavity by a Large Opening Situated Immediately in Front of the Sphenoid, and Behind the Still Cartilaginous Ethmoid. Nonpharyngeal Cephalocele. (Virchow.)

treatise (April, 1898), and citing three full pages of literature. He believes there are many different forms and a variety of causes, that even within one class there may be special individual modifying causes. The etiology of hydrencephalocele is probably the same as that of hydrocephalus, but acting in a limited area. In other varieties, hydrocephalus, new growth, hygroma of meninges (Virchow), amniotic adhesions, rachitic condition of bones, may all have a place in the etiology of special cases.

Clinical Features.—The cutaneous surfaces of the cephaloceles are usually smooth, more or less distended, and sometimes very vascular. Occasionally they are excoriated, or present old cicatrices. Angiomata and lipomata have been described as forming upon cephaloceles (Larger, Ried). Hydrocephalocele and meningocele exhibit a distinct sensation of fluctuation, while the encephaloceles have more of a sensation of softness and elasticity, but also show fluctuation if surrounded by a sufficient quantity of fluid. When the coverings are thin, from great tension by fluid contents, these tumors may be translucent. They frequently pulsate synchronously with the cardiac and respiratory movements; and their tension is often variable, as there may be a sinking of the tumor in sleep, and marked bulging out in the acts of crying or coughing. They may sometimes be diminished in size by pressure, which if moderate does no harm, but if great not infrequently produces symptoms of brain compression, such as vomiting, retardation of the pulse, unconsciousness, and convulsions. Pulsation is, as a rule, absent in meningocele and hydrocephalocele, but this naturally depends directly upon the size of the hernial opening in the skull, and the intercommunicability of the contents of the sac with those of the cranium; these tumors also show generally little variation during sleep, coughing, or crying, or upon the application of pressure, unless the hernial foramen is large. Symptoms depend to a great extent, too, upon the physiological value of parts protruded; and l in cephaloceles such parts are often very different from their analogues in the normally developed brain. In the light of the recent discoveries in cerebral localization these cases might often afford very interesting results by careful study.

Prognosis.—Many children affected with meningocele or hydrocephalocele die before or during birth. Sometimes the tumor bursts during parturition. Those born living rarely last many years, partly on account of the imperfect conditions of their brains, and partly because the tumor often rapidly increases to such size, by the superaddition of cerebrospinal fluid, that it bursts spontaneously, causing death either speedily, in coma or convulsions, or slowly, from a consecutive meningitis. Recovery after such evacuation of the tumor takes place but rarely. Death occurs usually in the first two or three years of life, but a few children with meningocele have attained the age of twelve, and even seveneth years.

The encephaloceles being smaller and simpler than the varieties just mentioned, still-birth and rupture are less common in cases affected with them, although they do occur. As a rule, this class either grows slowly or remains stationary. Whatever disturbance is excited is due to disorder of brain function, but patients suffering from the frontal variety live longer and with fewer cerebral symptoms than those afflicted with the occipital variety. Children with occipital encephaloceles are generally idiots, whereas with the frontal or sincipital tumors they are more commonly of quite normal intelligence. Many have reached adult age. In such cases hemiplegia, epilepsy, and optic atrophy have been observed.

Spontaneous recovery from encephalocele and meningocele has occurred, according to the observations of Wernher, Textor, von Bruns, and Held, by closure of the cranial defect and the complete isolation of the tumor as a cyst on the outside of the skull. Operative procedures have proved successful in some instances.

Diagnosis.—Every tumor of congenital origin situated along the median line of the head, in the region of the root of the nose, or in the glabellar or occipital regions, should excite suspicion of a cephalocele; and defects or malformations in other parts of the skull or body would be corroborative evidence. The fact of its being congenital must first of all be determined; then its relation to the various cranial sutures. The diagnosis is easy when the tumor is in one of the situations that have been described, when there are pulsation and a sensation of fluctuation, when there is a change in tension during sleep or in crying, and when there is a recession of its contents into the skull upon pressure. If, at the same time with the recession of the brain substance or cerebrospinal fluid, symptoms of irritation or compression of the brain develop, if there is an increase in the pulsatory or respiratory brain movements, and particularly if the edges of the hernial opening in the skull can be felt, a cephalocele is certainly present. The *x*-ray may be of value in indicating the size and position of the cranial defect. But sometimes most of these pathognomonic symptoms are absent, and the diagnosis can be made only from the seat and history of the tumor. Although seldom necessary, a fine aseptic hypodermic needle may be introduced to determine the character of the contents and the presence or absence of an opening in the skull.

The recognition of these hernias in the occipital region is easiest, because other congenital tumors of similar form are of extreme rarity in this position; but

dermoids, angiomata, and sarcomata of prenatal origin may have their seat at the nasal root, in the frontal region, or at the inner canthus of the eye, and thus lead to confusion. In the case of these latter, the mode of development must be carefully studied, and note taken of variations in tension, compressibility, and pulsation, and of the appearance of cerebral symptoms upon pressure. Angiomata exhibit pulsation and tension changes, and may be often completely compressed, but without brain symptoms or the discovery of an opening in the skull. Pulsation and compressibility are lacking in dermoid tumors. Cranial sarcomata which are congenital, or which appear shortly after birth, may present brain symptoms on pressure; there may also be an opening in the skull which pulsates; and finally these growths may have a similarity of feel, but they grow much more rapidly than cephaloceles, and usually are wanting in the more characteristic symptoms of the latter. The differentiation of the varieties of cephalocele can be made from the peculiarities that have already been described. In nasopharyngeal varieties it is well to remember their occasionally close resemblance to nasal polypi.

Treatment.—The most difficult class to treat are the hydrocephaloceles, but measures can at least be taken to prevent sudden death by spontaneous rupture of the sac. This is still more important in meningocele and cephalocele if there is a rapid increase of fluid and tension, as a cure is possible in many of these cases. Equable pressure should be made by means of cotton batting and a bandage, care being taken not to produce brain symptoms by too strong compression. If the distention increases, puncture should be made with a hypodermic needle, with antiseptic precautions, and the fluid slowly aspirated—all of it if the tumor is small, but only a portion in the case of large sacs. Then cover with aseptic cotton and continue the compression. Puncture may be repeated at appropriate intervals. In many of the cases lumbar puncture would probably serve the same purpose. If rupture has already taken place, the antiseptic dressing and pressure bandage should nevertheless be applied. By this procedure rupture may be prevented, the tumor may be gradually diminished in size, and occasionally even dissipated. Youths or adults who are occasionally observed with stabile encephaloceles should wear protective plates properly curved, with bandages, and sometimes compression may be made use of, if it be deemed expedient to do anything, but great care is needed to avoid the production of brain symptoms. Puncture in simple encephaloceles is permissible only in cases of continual augmentation in size—no other operative procedure is advisable. This is about all that can be done without risk. In many cases in which incisions have been made into these tumors, through a mistaken diagnosis, the result has been death from meningitis. Puncture and the injection of iodine have been fatal, and would probably be of value only in small pedunculated tumors with hour-glass constriction of the sac.

Meningoceles are more amenable to treatment, as a rule, than the other forms of cephalocele. Occasional punctures, together with compression, have met frequently with good results. The stabile meningoceles should, as a rule, be let alone, because they communicate almost always with the cranial cavity. Annandale in one case ligatured the peduncle and removed the tumor, the child recovering completely in spite of an attack of measles. Thompson has also cured a case by ligation. Schatz cured a case by the gradual compression of a clamp applied to the sac. Sklifasowsky removed an occipital cephalocele from a nine-months child with a ligature, the result being successful. The procedure is permissible in proper cases under strictly antiseptic precautions. Many operations in these cases have been undertaken since the inauguration of the new era of brain surgery, and much can now be achieved in the treatment of congenital cephaloceles, guided by the light of the latest discoveries in cerebral localization and by our improved technique in craniocerebral operations, which was formerly impossible. Fenger[4] operated successfully on a nasal type, first removing the polypoid mass with the écraseur. There was free discharge of cerebrospinal fluid. The nostril was packed with iodoform gauze preparatory to radical operation to close the hollow peduncle. He then did an osteoplastic resection of the superior maxilla (as devised by von Langenbeck), and transfixed and ligatured the peduncle. Aspiration of the tumor for fluid had been twice negative. He considers that in this class extirpation should always be practised even if the

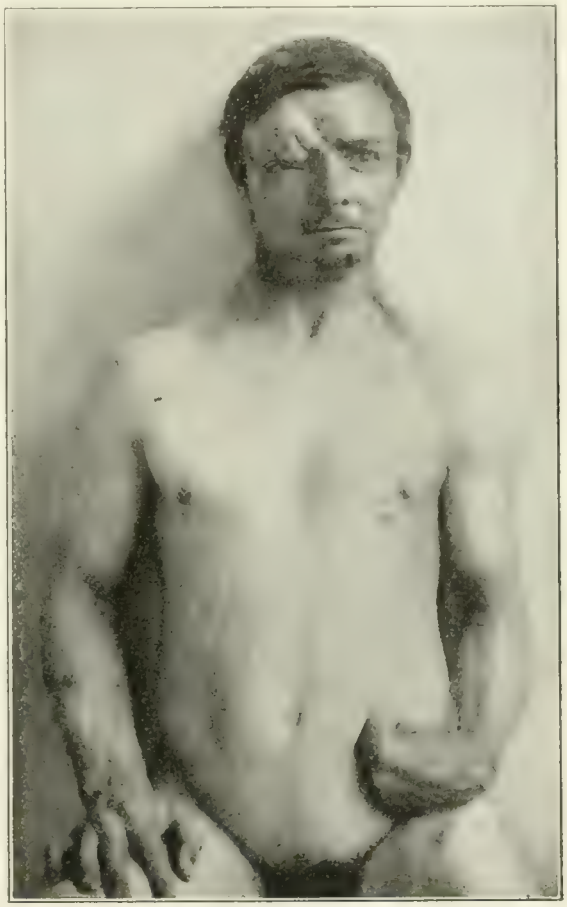

Fig. 1278.—A Case of Frontal Encephalocele. Man aged 30, mentally defective, with left hemiplegia and epilepsy. Radical operation for the relief of the defect had been performed at the age of 8. (Operation of Ramsay Hunt.)

tumor is small and causes no more disturbance than an ordinary polyp, as there is always danger of meningitis from accidental injury or surface inflammation. Preparatory operations are necessary, and these vary with the different situations in the nose.

Möller,[5] in an article on the surgical treatment of hydrencephalocele, says that the old rule of Heineke against operation has now been overthrown, since the day when von Bergmann openly advised radical operation wherever possible (1888). Möller cites the rules of de Ruyter (von Bergmann's assistant) as follows:

Meningocele should certainly be operated upon, because of possible ulcerations, because the tumor pre-

sents a point of lessened resistance in which a meningitis may originate, and because the patient is greatly burdened by the presence of the tumor.

Encephalocele should be operated upon unless it contains too large an amount of brain tissue. It usually holds a somewhat unimportant part of the brain, part of the occipital or frontal lobe.

Hydrencephalocele should not be operated upon because of its communication with a ventricle.

To combat this last rule of de Ruyter, Möller cites a case of successful operation on an occipital hydrencephalocele, where the tumor was nearly the size of the infant's head. The peduncle was solid, the lumen having been obliterated. Examination of the child one year after operation showed it to be in good condition and of apparently normal mental development.

Schmitz[6] reviews the forms of cephalocele and methods of operation, giving his experience of seventeen cases. He concludes that the permanent results of operation are very unsatisfactory. Life is prolonged, but in the case of hydrocephalocele, the child dies of hydrocephalus, or remains hydrocephalic. This he says is also true of meningoceles which show any signs of hydrocephalus. If there is no hydrocephalus, the prognosis is much better. Schmitz thinks the prognosis is best for the pure encephaloceles or solid tumors. It is important to note whether the tumor remains of original size or is disposed to grow, and whether it grows slowly or rapidly. In the latter case we must assume increasing intracranial pressure, and we have therefore a hydrocephalocele, or such a type is developing from the original encephalocele. Another question concerning the advisability of operation relates to the contents of the tumor. If sincipital, the middle frontal convolution is involved, and we may feel justified in removing a small portion. No motor and little mental disturbance will result. In the occipital class there is usually cerebellar tissue (hemisphere) and less frequently parts of the occipital lobe, and no symptoms are likely to follow removal of small peripheral portions of the cerebellum. In case of large prolapsus of brain substance, excision should not be practised.

Berger[3] believes radical operation to be justified in cases in which the tumor is growing and in which the prognosis is bad without interference.

Tilmann[7] says that the old methods of compression, puncture, iodine injections, and use of ligature are not now considered in the treatment of meningocele. Even if infection is avoided there is always danger of meningitis. He cites two cases of cephalocele operated upon at Bardeleben's clinic. The first was an occipital meningocele, the size of an apple, removed a few weeks after birth. The child developed normally. The tumor had a very small lumen and thick walls of edematous fibrous tissue. The second case presented a congenital occipital meningocele the size of the child's head. Operation was performed one day after birth because of insistence of the father. One liter of fluid was aspirated and the tumor sac was then removed. There was improvement at first, but the child died on the twenty-third day with paralysis and convulsions. The case was one of meningocele with chronic internal hydrocephalus. He discusses fully the methods of operation.

Acquired Cephalocele or Pseudocephalocele. — Among the cephaloceles which originate subsequently to birth, through disease of the cranial bones or subcutaneous fractures, the most common is the pseudomeningocele (or the chronic spurious meningocele of Billroth) as it is frequently called. This is observed almost exclusively in infancy or early youth, but, in very rare cases, sometimes in adults after healing of the superficial skull coverings in fractures. Conner[8] has written the best article upon pseudomeningocele that is to be found in American literature. Under the name traumatic cephalhydrocele he describes 2 cases occurring in his own practice, and makes an analysis of 22 others collected from general literature; 19 of these were due to subcutaneous fractures of the skull, 2 to old gunshot wounds of the skull and membranes where the scalp had reunited, and 1 was the result of trephining; 17 of the patients were under three years of age. G. Vivien has collected 8 cases, and Thomas Smith[9] reported 2, and described 20 analogous cases. All of Smith's were under sixteen years of age.

The history is usually that a child falls upon its head, and that, several hours or days after, a fluctuating swelling develops under the scalp, which may at first be diffuse, but later, as a rule, assumes the form of a sharply bounded cystic tumor. It may reach the size of the fist or be larger. It is over the injured part, fluctuates, and often pulsates. There is sometimes a hardened border to the tumor. Occasionally, by firm pressure, the fluid may be made to recede more or less completely into the skull cavity, when the fractured bone may be felt. When this is not possible, the break may often be felt after puncture and evacuation of the tumor. In many of these cases puncture has shown the contents to be cerebrospinal fluid. In postmortem examinations which have been made, the fluid has been found to lie under the pericranium, lifting it with its outer coverings like a cystic sac; a cleft is observed in the bone, and one of the same size or smaller in the dura mater, through which the sac and subdural cavity communicate. Occasionally the cortex has been injured, and in recent cases there would be signs of softening and of laceration of the other membranes. In a case of Lucas, the pseudomeningocele communicated with the open inferior horn of the left ventricle. Two or three cases may be mentioned in illustration of this traumatic form. Southam[10] gives the details in the case of a male infant, aged six months, that fell downstairs and sustained a subcutaneous fracture in the right parietooccipital region. Fourteen days later there was a swelling over the fracture, oval, soft, fluctuating, and pulsating. Moderate pressure was applied with a pad of lint and a bandage. In a month the swelling had disappeared and the child recovered. There was still a marked depression in the bone. Conner's first case was that of a boy twelve and a half years of age, who fell from a wagon, a wheel passing over his head. He was not unconscious, and walked into a house near by. There was a simple depressed fracture of the right half of the occipital bone, and a non-pulsating swelling over the fractured area, which was supposed to be due to extravasated blood. A week later, serum began to ooze from the nose, and there was puffiness of the right eyebrow. He punctured and drew off four ounces of a pale straw-colored fluid. The sac rapidly refilled, and four weeks later five ounces were removed. There were four subsequent tappings, the fluid withdrawn aggregating nineteen ounces. The specific gravity was 1.007; no albumin; sodium chloride, 6.6 parts per 1,000. The boy was never unconscious or delirious, but there were some insomnia and mental irritability, and the pulse ranged from 100 to 120. Conner's second case was in a hydrocephalic and rachitic colored child about two years of age who fell a distance of five feet upon its head. There was no scalp wound, but a swelling appeared very quickly over the right parietal bone. In a few days it measured four and a half by three and a half inches, and exhibited pulsation and fluctuation. A radiating fracture could be felt through the tumor. No treatment was undertaken, and nine months after the accident the swelling had disappeared.

There are several facts which explain the almost exclusive prevalence of traumatic pseudomeningocele in children. Possibly the flexibility of the skull gives a peculiar character to the fracture. The intracranial pressure is certainly relatively greater in children than in adults, and a more active secretion of cerebrospinal fluid is probably another factor. The increase in

subdural fluid may be due in part to the injury to the head, or in part to nutritive disturbance, rachitis, or some such thing, which does not give rise necessarily to a general hydrocephalus. The pouring out of the fluid, its augmented secretion, and the expansive power of the growing brain, all aid in preventing closure of the osseous fissure, and, indeed, may actually cause its enlargement, and even eversion of its edges. But pseudomeningocele is not a constant result of subcutaneous fracture in childhood, and it is likely that various causes and conditions conduce to its formation.

There are not many observations as to the further course of traumatic pseudomeningocele in children. Conner found that fifty per cent. of the cases collected by him died of meningoencephalitis. In some patients the tumor remains unchanged in spite of frequent puncture, and in others it is cured by this means. Spontaneous retrogression may take place. The cleft in the skull generally remains open, and hence the prognosis is always relatively unfavorable. These cases are often of considerable forensic interest. Bayerthal[11] relates the case of a man aged eighty-one years, with a pseudomeningocele still persisting, due to a brick falling upon his head when he was nine months old. The man was always normal, except that he did not learn to walk until four years of age, and that he developed epilepsy at the age of seventy-nine years. This is the only recorded case of such long persistence of a pseudomeningocele.

Pseudomeningocele in adults has been observed several times after gunshot wounds of the skull, when

Fig. 1279. Meningocele Spuria of Bullroth. (After Bayerthal, Centralblatt für die Grenzgebiete der Med. u. Chirurgie, October 11, 1905.)

the scalp wound was healed, and once after recovery with defect of bone from trephining. Vivien mentions three such cases. As a result of subcutaneous fracture in adults it has apparently not been observed, and, if it occurs, must be extraordinarily rare.

Pseudocephalocele sometimes results from syphilitic or tuberculous caries of the skull and perforation of the dura mater, and from complicated fractures accompanied with prolapsus cerebri.

These tumors vary from two to five inches in diameter, and are usually of a soft, elastic consistence. The skin over them is either smooth, glossy, and pale red, or inflamed, indurated, and presenting fistulous openings. Sometimes there are pulsations and fluctuation. Dizziness, retardation of the pulse, and even unconsciousness can, as a rule, be produced by pressure upon these tumors with the finger. Partial replacement may be brought about by compression, and in one case there was complete return of the hernia by gradual pressure. When the brain has protruded, this was doubtless due in many cases to the formation of cerebral abscess or to collections of pus in the cavity of the skull; in some cases, probably to edema or encephalitis with tumefaction of the brain in the neighborhood of the diseased or injured skull.

Treatment.—In pseudomeningocele continuous and equable pressure should be employed, when practicable, but this should be done early. If the tumor is large and tends to increase in size, operative interference is allowable, and this is best carried out according to the methods described by von Bergmann below. Strict antiseptic precautions should be observed, and a compress subsequently applied. Irritative injections are not advisable. If the opening in the skull remains patent, it is well to keep it shielded by a plate and bandage for the prevention of a renewal of the tumor or injury to the brain. Tonics, nutritious diet, and lime preparations are indicated.

Other forms of pseudocephalocele are treated according to the nature of the bone disease or injury. In suppurative processes we must be on the lookout for pus deposits in the brain or skull cavity, and remove them, if feasible, with careful asepsis. It is best not to operate on the prolapsed brain itself, but in this we must be governed by what we have recently learned with regard to the physiological value of the different convolutions. Hitherto such heroic measures have been carried out usually as a result of error in diagnosis, and in these cases death has followed from meningitis, encephalitis, or hemorrhage. Compression should naturally be resorted to in these cases only when there are no symptoms of inflammation or suppuration. In the rare pseudocephaloceles of adults we may cautiously puncture and make use of the compress, but we should always be on the lookout for symptoms of inflammation and abscess.

Bayerthal[11] advances the singular theory that the presence of a pseudomeningocele may be of *advantage* to the patient as a safety valve for increased intracranial pressure, and that it might be more advantageous to *enlarge* it, than to remove it, in cases showing cortical irritation.

Von Bergmann[12] (in an article on "Cephalhydrocele Traumatica") says that in these cases he always presupposes a fracture of the skull—in the majority of the cases of the lateral aspects of the skull—the lined fractures being vertical. The interval often observed between the bones in such cases is doubtless due to subsequent absorption. A laceration of the dura has always been found at autopsy. He considers compression of service only in a few cases, and only when applied early. Puncture is successful in a few; but meningitis is to be feared. In 33 cases of Rahm, where puncture was employed, 6 were cured and 9 died. Of 3 cases treated by puncture and iodine, 2 died and 1 recovered with prolapsus cerebri. Two cases treated by incision and drainage died. He cites Krönlein's two cases, in which the sac was removed and drainage employed. Both recovered. One had to wear a plate, and in the other epileptic convulsions returned seven to eight months after operation. Von Bergmann concludes as follows:

1. Puncture should not be practised. Injections with iodine are still more inadvisable.

2. Compression should first be tried (with compress and bandage or with a plate). If the tumor is thereby kept small and flat, radical operation can be delayed.

3. If the tumor increases in size, the method of Slajmer and Dembrowski is simple and less dangerous than the method of Krönlein. This consists of making a flap of skin, periosteum, and bone to cover the defect in the skull, first emptying the sac and dissecting it away from the edge of the bone.

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J. RAMSAY HUNT.

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Cephalometry.—See *Skull.*

Cera.—CERA FLAVA, *Yellow wax; Beeswax; Wax.* A solid substance prepared from the honey-comb of the bee (*Apis mellifera L.*). (U. S. P.)

Wax is an animal product secreted by bees under the rings of the abdomen, where it accumulates, when the insects are comb-making, in scales or flakes. These flakes are disengaged by the bees, and, with jaws and legs, moulded into that remarkable structure, the honey-comb. It appears to be an analogue of the sebaceous secretion of the skin. The wax is obtained by depriving the comb of its honey, chiefly by means of centrifugal apparatus, and is purified by melting one or more times in boiling water, straining, and cooling. It is then melted and cast in large solid cakes.

Wax is too familiar to need description, were it not for its very frequent adulteration, which unfortunately is not always easily detected. It is a yellowish or brownish-yellow solid, having an agreeable, honey-like odor, and a faint, balsamic taste. It is brittle when cold, but becomes plastic by the heat of the hand. It melts at 63°–64° C. (145.4°–147.2° F.), and congeals with a smooth and level surface. Specific gravity, 0.951 to 0.960 at 25° C. (77° F.) It is insoluble in water, but soluble in thirty-five parts of ether and in eleven parts of chloroform; also soluble in the oil of turpentine and in fixed or volatile oils. Cold alcohol dissolves it only partly, but it is almost completely soluble in boiling alcohol. Boiled with a solution of soda, wax does not saponify like the fats and resins, and their mixture with wax can be detected in this way; if the liquid so boiled, after the wax has been separated by cooling, remains turbid, or gives a precipitate when acidulated with hydrochloric acid, fat, resin, soap, or something of that kind is present. If five grams of wax be heated, in a flask for fifteen minutes, with twenty-five grams of sulphuric acid, to 160° C. (302° F.), and the mixture diluted with water, no solid, wax-like body should separate (absence of paraffin).

The most common indication of adulteration is a concave upper surface of the cake. About ninety per cent. of the beeswax consists of *Cerin* (*Cerotic acid*, $C_{27}H_{54}O_2$), the remainder being chiefly *myrical palmitate.* Variable accidental constituents, depending upon the geographical source, and special conditions, exist in small quantity.

CERA ALBA, *White wax; Bleached wax*, is "yellow wax, bleached." (U. S. P.) White wax is usually prepared by being cut into thin ribbons or shreds and exposed for a few weeks to the atmosphere and sunlight, being also frequently watered. It may also be bleached by the less desirable method of treatment with the oil of turpentine or some chlorine solution. It is a yellowish-white solid, somewhat translucent in thin layers, having a slightly rancid odor and an insipid taste, answering otherwise nearly to the description and tests given above.

ACTION AND USES.—Wax is insoluble in the body, and therefore exerts only a mechanical action upon it. Its use internally is entirely obsolete. Formerly it was occasionally recommended for diarrhea or dysentery, and later, as a pill-coating. Its plasticity and very great permanence make it useful as a temporary tooth-filling where the cavities are tender and away from the grinding surfaces. Its principal employment in medicine, however, is as a component of cerates (which derive their name from it), plasters, and ointments, to which it gives durability and consistence. It is perfectly non-irritating.

The most important uses of wax are ceremonial and domestic—candles and mechanical moulding and modelling.

ALLIED SUBSTANCES.—Chinese wax, secreted by Coccus ceriferus upon a Chinese ash; a hard, translucent, spermaceti-like substance; Japanese, from the surface of the fruits of several species of Rhus; bayberry wax and several other vegetable products. See also *Cetaceum.*

H. H. RUSBY.

Cerata.—A cerate (*ceratum*) is an unctuous solid preparation resembling an ointment, but of a firmer consistence. Cerates are softer than plasters, are easily spread upon muslin or other substance with a spatula, and do not melt and run when applied to the skin. Cerates are made of wax (L. *cera*) with oil or lard; it has been found that those made with yellow wax keep better than those made with white wax. They should be kept in a cool place.

CERATES OF THE U. S. PHARMACOPŒIA AND NATIONAL FORMULARY.

CERATUM (Simple cerate).....	U.S.P.	White wax 30, white petrolatum 20, benzoinated lard, 50.
C. CAMPHORÆ (Camphor cerate).	U.S.P.	Camphor liniment 10, white wax 35, white petrolatum15, benzoinated lard 40.
C CAMPHORÆ COMPOSITUM (Compound camphor cerate; camphor ice).	N.F.	Camphor 10.7, white wax 15, castor oil 25, spermaceti 48, phenol 0.2, oil of bitter almond 0.1, benzoic acid 1.
C. CANTHARIDIS (Cantharides cerate).	U.S.P.	Cantharides 32, liquid petrolatum 15, yellow wax 18, rosin 18, lard 17.
C. CETACEI (Spermaceti cerate).	N.F.	Spermaceti 10, white wax 35, olive oil 55.
C. EXTRACTI CANTHARIDIS (Cerate of extract of cantharides.)	N.F.	Cantharides 30, rosin 15, yellow wax 35, lard 35, alcohol q.s.
C. PLUMBI SUBACETATIS (Cerate of lead subacetate; Goulard's cerate).	U.S.P.	Solution of lead subacetate 20, wool fat 20, paraffin 20, white petrolatum 38, camphor 2.
C. RESINÆ (Rosin cerate; Basilicon ointment).	U.S.P.	Rosin 35, yellow wax 15, lard 50.
C. RESINÆ COMPOSITUM(Compound rosin cerate; Deshler's salve).	U.S.P.	Rosin 22.5, yellow wax 22.5, prepared suet 30, turpentine 11.5, linseed oil, 13.5.
C. SABINÆ (Savine cerate)....	N.F.	Fluidextract of savine 25 rosin cerate 90.

R. J. E. SCOTT.

Ceratixodes.—A genus of ticks, *Ixodinæ*, that is parasitic on sea birds, and individuals of its only species, *C. putus*, are often found on cliffs. The palpi are long; eyes absent; no anal groove in female; stigmata circular; one anal and two adanal shields in male. See *Arachnida*. A. S. P.

Ceratophyllus.—A genus of fleas, family *Pulicidæ*, in which there are ctenidia on the prothorax but not on the head. These insects are parasitic on rats and mice and may carry disease. See *Insects, Parasitic*. A. S. P.

Cercaria.—A larval stage in the development of trematode worms. A cercaria usually possesses a ventral sucker in addition to one at the mouth, a triclad digestive tract, and a tail for swimming. It is really a young distome, which either enters its final host directly or becomes encysted for a time before being finally transformed into an adult fluke. See *Trematoda*. A. S. P.

Cercomonas.—A genus of flagellate protozoans, family *Cercomonidæ*, with a large flagellum and no undulating membrane. Species of this genus have been found in the alimentary canal, bronchial system, pleural exudates, and in echinococcus cysts. Their associations in the human body are not well understood. See *Protozoa*. A. S. P.

Cerebellum, Anatomy of.—See under *Brain*.

Cerebellum, Disorders of the.—The cerebellum is a highly complex structure. Its chief function is that of automatic orientation of the bodily movements in time and space. Disturbances of its incoming and outgoing pathways produce for the most part conflicts with the laws of gravity, which are compensated for by equilibrium movements. The loss of the control of time, as well as of space relations, causes uncertainty and inaccuracy of movements, and this gives rise to a number of motor anomalies, which may involve almost any series of voluntary muscles of the body. So far as is yet known, none of the sympathetic structures seem to be implicated in cerebellar disturbances.

A clinical study of the cerebellar syndromes shows that not only does one have to reckon with lesions within the cerebellum itself, but also, by reason of its position within the cranial cavity, pressure from objects lying in contiguous structures may bring about disturbances of cerebellar functions properly so-called. Furthermore, the close anatomical relations with the structures of the midbrain, the red nucleus, the optic thalamus with important centers in the medulla and the pons, and also the cord, need to be borne in mind in any analysis of disturbances of the cerebellar functions. (Fig. 1280.)

The cerebellum has been termed by Sherrington the chief organ of coordination, and the reflex system of the proprioceptors. It receives impressions from a great variety of receptors throughout the body. Concerning many other receptors and their pathways nothing is known as yet nor is it yet definitely established that they pass by way of the cerebellum to the cortex. Receptors for heat, for cold, for touch, for weight, for pain, sound, light may have representation to a greater or less degree within the cerebellum but this is still unproven. In general one may say that the cortex of the cerebellum is largely a sensory organ, but sensory only in a special sense, that is, with reference to the receptors governing movements working with time and space relations. Some authors refuse to call this sensory. From the cerebellar cortex impressions, for the most part, are distributed to the internal cerebellar nuclei from which apparently the chief motor impulses proceed. (Fig. 1281.) These nuclei are the dentate nucleus, Deiter's nucleus, nucleus globosus, nucleus emboliformans, and the nuclei of the tegumentum.

The chief incoming pathways traverse the three cerebellar peduncles. Bechterew summarizes these somewhat as follows:

1. *Inferior Cerebellar Peduncle Paths.*—(*a*) The Flechsig column, or the dorsospino-cerebellar tract. This passes up the lateroventral side of the lateral column, originating from cells in Clark's column. It is distributed to the middle lobe of the vermis, and the ventrolateral lobe of the lobus centralis.

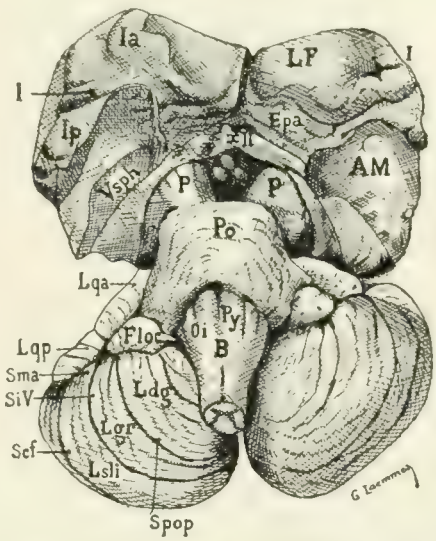


FIG. 1280.—Lower Surface of the Cerebellum. AM, anterior wall; B, medulla; Cv, hemispheres of the cerebellum; Epa, anterior perforated space; Fe, bundle of Féré; Floc, flocculus; I, insula; i, fissure of the insula; Ia, anterior convolution of the insula; Ip, posterior convolution of the insula; LF, frontal lobe; LT, temporal lobe; Lc, central lobe; Ldg, digastric lobe; Lgr, lobus gracilis. (Thomas.)

(*b*) Columns of Gall and Burdach send fibers from the nucleus gracilis and nucleus cuneatus dorsally, and uncrossed, to the inferior vermis, ventrally, and crossed, to the superior vermis. (*c*) Olivocerebellar tracts, originating in the cord, passing by way of the inferior olivary bodies directly to Deiter's nucleus, and crossed to the superior vermis. (*d*) An important path is the vestibulocerebellar path from the vestibular ganglion to Deiter's nucleus and thence to the inferior vermis. Other pathways are described but those mentioned stand out foremost.

2. *Middle Cerebellar Peduncle.*—This receives fibers coming from the pontine nuclei, located in the pontine reticulum and the ventrolateral pontine nuclei. Some of these fibers appear to be directly associated with the corticopontine tracts, and it is through them that many of the frontal impulses pass which aid in the conscious control of disturbed equilibrium, as well as constituting a higher reflex pathway.

3. *Superior Cerebellar Peduncle.*—At least four incoming sensory tracts are described. That which is best known is the column of Gowers, which also originates in the column of Clark and passes into the cerebellar cortex.

Incoming fibers from the red nucleus (rubrocerebellar) and from the thalamus (thalamocerebellar) make up others of the superior cerebellar tract sensorimotor system.

The chief *motor pathways* from the intrinsic nuclei of the cerebellum pass out through the superior

cerebellar peduncle. Hence lesions of the superior cerebellar peduncle are of special moment in determining the symtomatology of cerebellar disease. These pathways are variously known as the cerebellorubral and cerebellothalamic tracts. The cerebellum thus forms an important sensori-motor station in a complicated series of reflexes which, so far as the cerebellum is concerned, work automatically. The cerebellar cortex acts as a primary reception station and the intrinsic

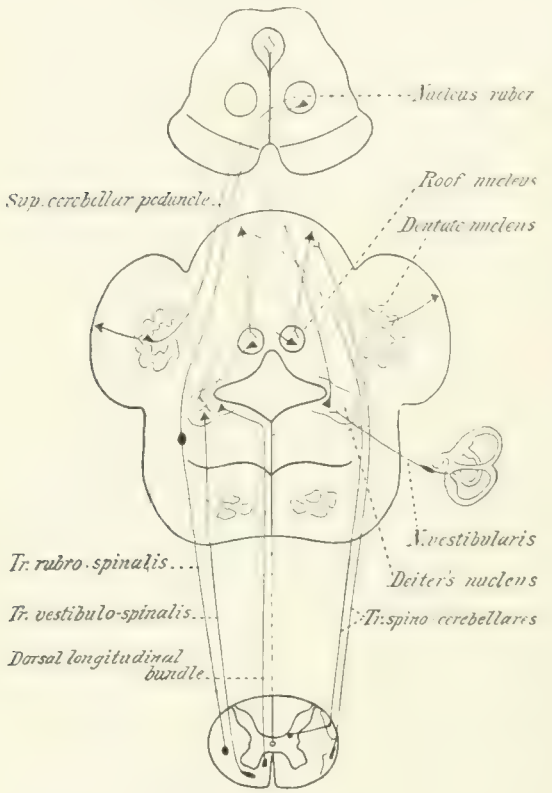


Fig. 1281.—Illustrating Spinal Connections with the Cerebellum. Incoming paths on right, outgoing paths on the left. (Holmes.)

nuclei as the primary motor impulse originating sources. The sensory impulses going through the cord and brain stem traverse the paths just enumerated and convey information chiefly concerning the states of tension of the muscular parts of the extremities, the trunk, the head, and the muscles connected with the organs of special senses; states of pressure in the joints; or facts concerning states of pressure upon the skin; possibly states of pressure on the viscera within the body.

To this purely reflex mechanism, which, roughly speaking, may be sketched as consisting of afferent paths to the cerebellum, efferent paths to the red nucleus and down the spinal cord, is added the controlling cerebral system largely through the frontopontocerebellar paths. The accompanying illustrations from Holmes in White and Jelliffe's Modern Treatment of Nervous Mental Diseases, Lea and Febiger, 1913, show the chief spinal and cerebral pathways both afferent and efferent (Figs. 1281 and 1282).

Symptomatology.—The general symptoms of cerebellar disturbances, or of diseases or disturbances of its connections therefore offers a multitudinous complex, the details and anatomical correlations of which are still being rapidly added to at the present time. Certain cardinal symptoms are capable of partial analysis and point with a fair degree of distinctness toward cerebellar disease.

Cerebellar Ataxia.—This complex classical sign of cerebellar disturbance consists in disturbance of coordination of the larger muscular group actions, the trunk and lower extremities being chiefly involved. The head, eyes, and upper extremities may be affected. Signs of distinct paralysis are absent.

The making of fine coordinated movements, standing and walking, are interfered with. In the severe grades, standing, and in some cases even sitting, become impossible. In walking, the wabbly, side-stepping, drunken gait, named for Duchenne, and described by him and other French authors, is extremely characteristic. Stewart and Holmes, in a partial study of the cerebellar gait (*Brain*, 1904) show two characteristic trends of disturbance: first, staggering lateropulsions toward the affected side, backward or forward, according to the location of the lesions in vermis or dentate nucleus. The patient feels as if he were pushed to one side, and in attempting restitution overcorrects, thus producing the swaying movement. Second, the entire orientation in space is influenced, the patient bending in the direction of the affected side. The characteristic menagerie-like movements result from conscious attempts at correction (frontocerebellar paths), producing the larger zigzags in the general course of progression. Forward and backward movements have their special localizing signs. (Figs. 1283, 1284, 1285, and 1286.

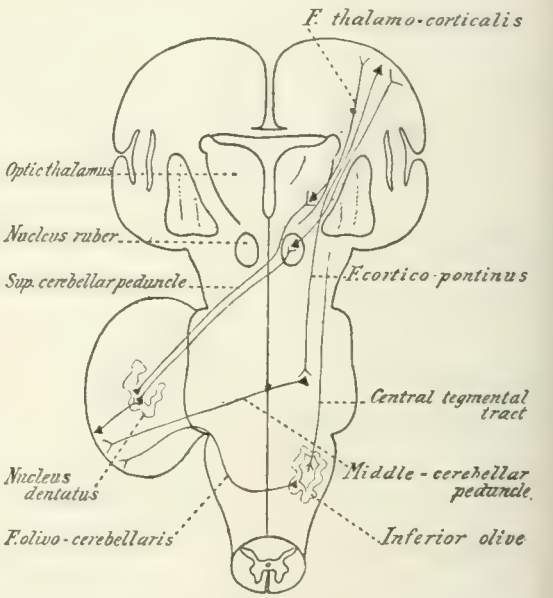


Fig. 1282.—Illustrating the Afferent and Efferent Connections of the Cerebellum with the Forebrain. (Holmes.)

Cerebellar ataxias may be the result of involvement of the spinocerebellar paths (Flechsig, Gowers, vestibular system), as in the Freidreich-Marie ataxia group (see Fig. 1281); they may arise from involvement of the superior cerebellar peduncles—from bulbar and pontine involvements of these paths, and from implication of the cerebellorubral, cerebellothalamic, and frontocerebellar paths. (See Fig. 1282.) Typical cerebellar ataxias, with drunken gait (Burns, Oppenheim), are seen in some cases of frontal tumor. The accompanying localizing disturbances, and dissociative (diaschitic) signs of the disturbed cerebro-

Fig. 1283.

Fig 1284.

Figs. 1283 and 1284.—Cerebellar Ataxic Gait. Lesions in the inferior cerebellar peduncle and in the medulla. See Figs. 1287 and 1288. (Thomas.)

Fig. 1285.

Fig. 1286.

Figs. 1285 and 1286.—Cerebellar Ataxic Gait in Different Positions from Those Shown in Figs. 1283 and 1284. (Thomas.)

cerebellar paths should be taken into consideration in differential diagnosis.

The ataxias (dysmetrias) of the upper extremities, associated with ataxias of the trunk and lower extremities in standing, walking, etc., are chiefly bilateral, unilateral, or lateral (usually homolateral). The influence on the ataxia of the absence or presence of visual aid is but slight, or none at all, as shown by the finger-finger and finger-nose test. Owing to

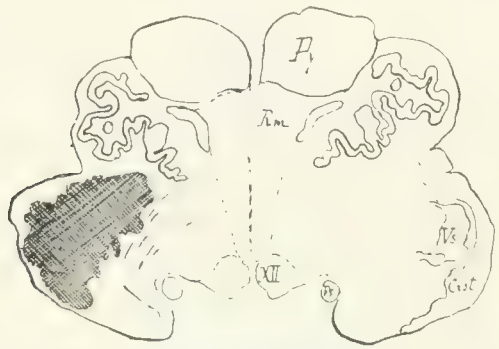


Fig. 1287.—Lesion in the Restiform Body (Inferior Cerebellar Peduncle) in the Patient Shown in Figs. 1283, 1284, 1285, and 1286. (Thomas)

the poor coordination of the individual muscular activities, the desired act, as in walking, can be performed only after several trials and errors.

Nystagmus.—This collection of eye movements is almost invariably present in cerebellar path disturbance, and being closely related to the vestibular system may be the result of either intracerebellar or extracerebellar implication of these paths. True vestibular nystagmus is almost invariably accompanied by vestibular vertigo and ataxia. It is modified by the position of the head, and examination should therefore be carried out with the head in each of the three planes. A patient with vestibular nystagmus tends to rotate within the plane of the nystagmus, and in the direction opposite to that of the quick nystagmic movement; thus, a patient with vestibular nystagmus who bends his head forward ninety degrees will rotate in a direction directly opposite if he bend his head backward ninety degrees. The laws of intracerebellar nystagmus apart from actual vestibular disease remain to be investigated. Skew deviations (Fig. 1289), and other eye displacements are to be interpreted in the light of forced movements having their analogies to nystagmus. They point to involvement of the middle cerebellar peduncle often. Nausea, vomiting, amblyopia, loss of consciousness, and pain in the muscles of the neck are closely associated with disorder of the vestibular system.

To separate true cerebellar nystagmus from labyrinthine nystagmus is not always possible.

Holmes states that nystagmus is a common and very valuable localizing sign of local cerebellar lesions. It is almost certainly a true cerebellar symptom, though Bing is quoted as regarding it as an effect of the pressure of the cerebellar disease on the abducens nucleus, or on the dorsal longitudinal bundle. It is rarely observed on direct forward fixation of the eyes, except with severe and acute lesions and generally appears only on lateral or more rarely on vertical movements. When the cerebellar disease is unilateral the nystagmus is most marked on conjugate deviation of the eyes toward the side of the lesion, and consists of a relatively slow forcible jerking movement in this direction and a gradual recession toward the middle line. On conjugate deviation toward the opposite side the nystagmoid movements are more rapid, but smaller in range. The nystagmus is almost invariably conjugate, *i.e.* the eyes move simultaneously and equally. Nystagmus is less commonly associated with vertical movements of the eyes, and when it occurs is generally rotatory, in the direction of the movement and toward the side of the lesion. Barany's observation tends to show that the suppression of calorific nystagmus associated with spontaneous nystagmus, indicates a central lesion in the cerebellum or pons Varolii.

Nystagmus is much more common in acute than in chronic cerebellar disease: it is rarely prominent in the slowly progressive atrophies.

Adiadochokinesis.—This symptom, which was originally described by Babinski as characteristic of cerebellar disease, consists of a disability to perform rapidly alternating agonist and antagonist movements, such as rapid pronation and supination, finger play, etc. While not invariably found, nor always clearly indicative of cerebellar path involvement, its presence is of sufficient frequency to ask for special mention. It is only a variant of a special ataxia brought out by a special test, and where paralysis is absent points to involvement of the cerebellar paths. It is frequently absent in extracerebellar tumors (frontal tumors) in which other well-marked cerebellar signs are present. It is an extremely important sign and its presence should always be sought for. It is very frequently found in chorea and in paralysis agitans, thus indicating certain localizing signs in these disorders so often, but erroneously, spoken of as functional nervous disorders.

Fig. 1288.—Lesion in the Medulla in the Patient shown in Figs. 1283, 1284, 1285, and 1286. (Thomas.)

Vertigo, generally of a rotatory character, is usually a conspicuous sign in disorders of the cerebellum. It occurs most frequently in tumor or abscess. The patient not only may feel himself revolving in space, but objects may appear to revolve from right to left, or from left to right. Vertigo of an up or down character appears more rarely and has been thought to obtain in tumors in the anterior vermis which being close to the corpora quadrigemina press upon

these structures. The character of the vertigo must be sharply enquired into. The symptom arises chiefly from lesions connected with the vestibular paths, as the labyrinth is the chief cephalic ganglion in the proprioceptive systems, of which the cerebellum constitutes the coordinating center, and disease of the labyrinth itself, as well as of its extracerebellar and intracerebellar paths may cause vertigo. Differential diagnosis between labyrinthine disease and intracerebellar disorder is possible as a rule by means of the Barany tests.

Stewart and Holmes point out that accumulation of experience shows that as a general rule objects rotate

Fig. 1289.—Patient with Skew Deviation of the Eyes. The right eye looks up and out; the left eye down and in. Patient with a tumor of the lateral lobe of the cerebellum. (Holmes.)

from the diseased to the well side in intra- as well as in extracerebellar disturbances, whereas the subjective sense of rotation is usually from the diseased to the well side in intracerebellar disorder, and the reverse in extracerebellar involvement of the paths. Further study is needed on this point.

Cerebellar hypotonus, usually one-sided, may be present in cerebellar affections. It is revealed by palpation of the muscles, testing of resistance movements, and looseness in performance of passive movements. This hypotonia or atonia is usually accompanied by normal or even exaggerated tendon reflexes, as contrasted with that of peripheral neuritis or tabes. It is present only in more acute lesions to any great extent. Stewart and Holmes have noted a striking feature of this hypotonus. The extensor recoil, which ordinarily follows the sudden flexor jerk induced by the sudden relaxation of resistance to a definite movement is almost always absent in a cerebellar hypotonic reaction, whereas the flexor jerk itself is excessive. They test it as follows: the patient is asked to place his elbow on a table or other rest and to flex his forearm as strongly as possible, the observer resisting the movement by grasping his wrist. When the wrist is suddenly released the forearm rapidly flexes for a short distance, but if the limb is normal it is quickly brought to rest by the sudden reflex tonic contraction of the antagonists of the contracting muscles, *i.e.* the triceps; and if the limb is spastic there may be a considerable recoil. In cerebellar hypotonia, on the other hand, the movement is not checked by this reflexly excited contraction of the triceps and the forearm continues to move until flexion is no longer physically possible.

Asthenia.—Although the presence of asthenia in cerebellar disorder has been interpreted as being due to a lesion of the pyramidal tracts by contiguity, it is unquestionably a true cerebellar symptom. It is usually homolateral to the lesion, and is closely related to cerebellar hypotonus. It occurs particularly in acute lesions and is transient. The limbs are often tremulous and the head if unsupported may sway from side to side in small oscillations. Disorder of the tractus cerebellovestibularis spinalis, or rubrospinalis usually gives rise to this symptom.

Cerebellar Asynergia.—This is a severe grade of retro- and propulsion, as seen in paralysis agitans, both being due to similar pathological foundations. The patient is totally unable to balance himself, so that either his legs walk away from under him, or he pitches forward without their following. The condition has been described by Babinski as being a special symptom of cerebellar disease, whereas in reality it is one of the components of cerebellar ataxia, but in the anteroposterior plane rather than in the lateral

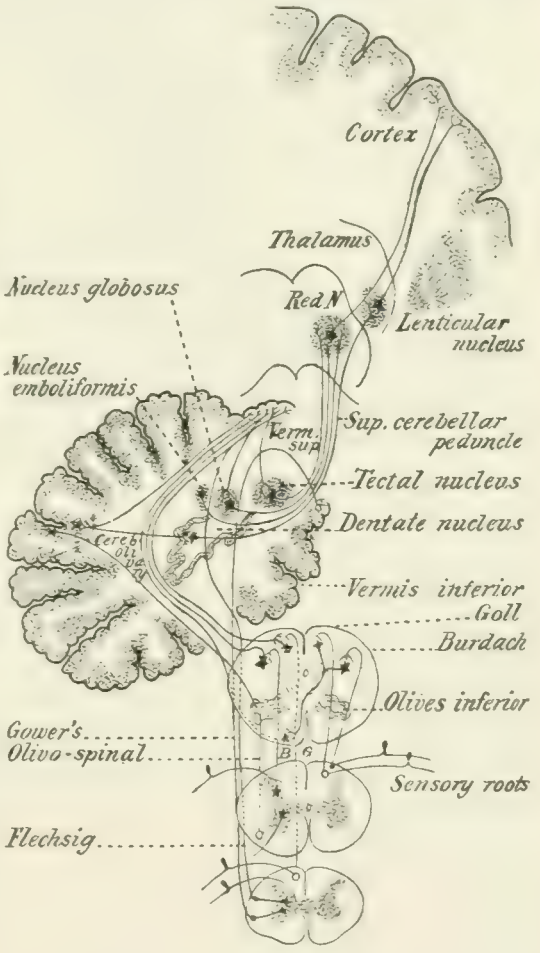


Fig. 1290.—The Chief Cerebellar Paths, as Given by Bechterew.

planes. If a normal person be requested to place one foot on a chair in front of him he does so by simultaneously flexing his hip and knee; a patient with cerebellar ataxia will, however, probably first raise his leg by flexing his thigh, and only later flex his knee; the two acts are not simultaneously executed. Similarly, though the patient may have difficulty in maintaining his equilibrium as he walks he does not aid himself by swinging his arms in association with the movements of his legs. Another test of asynergia,

which well illustrates its effect on gait, is to ask the patient to throw his head backward; in attempting this he may fall owing to failure to readjust his balance by the simultaneous flexion of his knees. To this asynergia the difficulty in equilibration is largely due. Movements which displace the center of gravity, as every step must do, do not excite reflexly the normally associated muscular contractions, which again throw the center of gravity over the base; in other words the body does not adjust itself immediately to its altered position.

Fig. 1291.—Paralysis of Upward Movement of the Eyes; showing the excessive wrinkling of the forehead in the attempt to look up. (Holmes.)

Forced Movement.—Forced movements of the muscles of the neck and eyes are present in cerebellar disorders and appear as irritation or as defect symptoms due to disease of the hemispheres or of the middle cerebellar peduncle.

Ocular movements are more characteristic. Ocular palsies are not a direct result of cerebellar disease, though they not infrequently occur in cases of tumor or abscess owing to pressure transmitted directly or indirectly to the nuclei of the ocular nerves. Thus the sixth nerve suffers the most frequently, but tumors in the anterior part of the vermis may produce a palsy of the trochlear, or of some part of the oculomotor nerve. Weakness of lateral conjugate movement of the eyes toward the side of the lesion is probably also only an indirect effect. The "skew deviation," originally observed by Magendie, seems, however, to be attributable to the disease of the cerebellum itself as well as to middle cerebellar-peduncle lesion, as has been noted.

Speech Disturbances.—Dysarthrias are usually present in defects of the cerebellum, and may point to general defect of the entire organ, disease of the bulbocerebellar tracts, or pressures upon the bulbar nuclei from contiguous new growths. They are usually symptomatic of the same type of ataxia as found in the other muscles of the body (adiadochokinesis).

Cerebellar Fits.—Tetanus-like convulsive seizures, with characteristic holding of the body in extended rigid position, originally described by Jackson in 1871. (Fig. 1292.)

From the *clinical point of view*, disorders of the cerebellum are best discussed in the following order: (1) Those of the peduncles; (2) disorders of the cerebellum itself; (3) disorders of extracerebellar location, with implication of the cerebellar functions in the posterior fossa, and having additional symptoms caused by pressure on contiguous structures—pons, medulla, fourth ventricle.

1. Lesions of the Peduncles.—*Inferior Cerebellar Peduncle; Corpus Restiforme.*—Whereas disorders caused by pressure due to pontine or bulbar diseases are not infrequently met with, isolated disease of the inferior peduncle itself is very rare. The coordinating path, *i.e.* cerebellovestibulo-spinal tract is chiefly involved. The most striking symptoms are turning of the body toward the site of the lesion, vertigo with tendency to fall in the direction of the side of the lesion, forced positions, and modifications of the eye movements (convergent and divergent strabismus, occasionally skew deviations). Adler has digested the literature. (Die Symptomatologie der Kleinhirn-Erkrankungen, Weisbaden, 1899.)

Lesion of the Middle Cerebellar Peduncles.—This is rarely seen without complications, and lesions of the pons frequently give rise to symptoms by implicating the middle peduncle. The characteristic symptoms are rolling movements of the body on its vertical axis, skew deviation of the eyes, Magendie-Hertwig syndrome (one eye showing higher than the other). The patients behave as though they had bilateral vestibular disease, causing the rolling motions. The eye symptoms are caused by lesions of the fasciculus anteromarginalis, fibers to the posterior longitudinal bundle and interference with the fibers to the abducens nucleus.

Lesions of the Superior Cerebellar Peduncles.—It is also very rarely that these are met with without

Fig. 1292.—Position of the Body in a Cerebellar Fit. (Jackson.)

complications. Nystagmus has been observed, but ocular implications are not the rule. The choreic or paralysis agitans-like tremor, appearing on the same side of the lesion, which is so characteristic, may be due to implication of the cerebellorubrospinal bundle. Forced positions of the head to the side of the lesion have been described.

Here the relationships to the midbrain are very close. (See *Midbrain*, under *Brain*.) Tremor is a most characteristic topographical sign of disease of these paths in the midbrain. This fact was first pointed out by Benedikt and the coexistence of unilateral tremor with paralysis of the opposite third nerve has become known as the syndrome of Benedict. (See *Benedict's Syndrome.*) The tremor often resembles

very closely that of paralysis agitans; it is relatively regular in rate, range, and amplitude, and of a frequency of three to five oscillations per second. It occurs as a rule only when the limb is wholly or partially unsupported. It is not under volitional control, and it generally becomes a well-marked intention-tremor on movement. Occasionally the spontaneous movements are more irregular or choreiform, and even athetosis may occur, but this is more characteristically associated with lesions of the optic thalamus than of the midbrain. (Fig. 1294.)

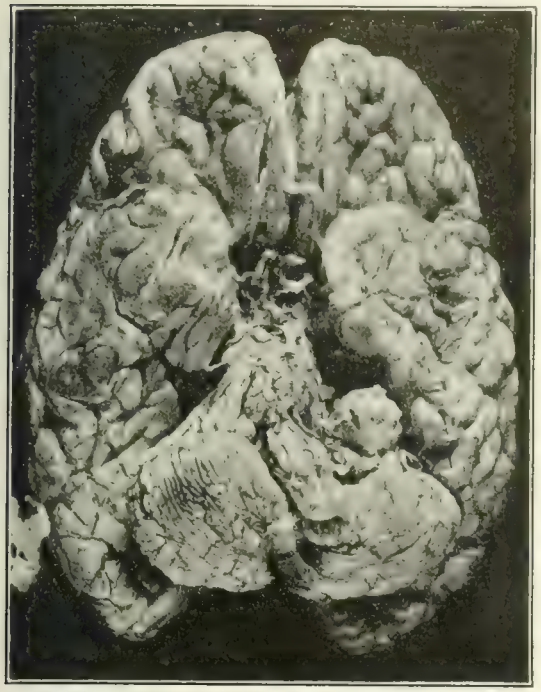


Fig. 1293.—Tumor of the Cerebellopontine Angle, with Atrophy of the Middle Peduncle of the Cerebellum.

The exact pathogenesis of these spontaneous movements has been much discussed. The original view favored by Charcot and others, writes Holmes, attributed them to a partial or irritative lesion of the pyramidal tract, but numerous facts disprove this hypothesis; it is indeed now recognized that in order that they occur it is essential that the pyramidal tract should not be severely injured. On the other hand many facts tend to prove that tremor may result from a destructive lesion of any part of the superior cerebellar peduncle, or of the nucleus ruber in which it terminates, or of the rubrospinal tract or Monakow's bundle which passes from this to the spinal cord. It therefore seems to depend on a lesion of the cerebellorubrospinal system when the pyramidal tracts are relatively intact (Bonhoeffer, Holmes). If this be so the tremor must be homolateral to the lesion if the cerebellar peduncle is affected before its decussation, contralateral if the lesion lies above the decussation or involves the nucleus ruber, and again homolateral if its affects the rubrospinal tract after its crossing. In the majority of cases in which it depends on involvement of the nucleus ruber it is generally found on the same side as the sensory and motor disturbances and on the side opposite to the lesion.

This tremor is generally associated with hypertonicity of the muscles and rigidity of the limbs, and this increases the danger of confusion of these cases with paralysis agitans. Sometimes, indeed, the face too is rigid and mask-like.

Symptoms of Chronic Cerebellar Disease.—As Holmes has well shown, the symptoms which supervene on acute cerebellar lesions gradually diminish with time, and may in part disappear. Those symptoms which characterize chronic or slowly progressive disease of the cerebellum are represented by the systemic atrophies and degenerations of the cerebellum, as well as by old softenings and hemorrhages and by neoplasms that have become latent. In these cases it frequently happens that the symptoms are much less marked than might be expected from the severity and extent of the disease.

The disturbances of movement are invariably the most pronounced, and it is especially gait that is affected. Though the individual and simple movements of the upper extremities may be executed fairly well, or may show at the most only a moderate degree of ataxia, the more complex acts which require the coordinated and synergic cooperation of many groups of muscles are generally grossly ataxic. Gait is consequently as a rule very severely affected, and may show all the characters of that described as a result of acute cerebellar lesions. The patient reels and staggers from side to side as a drunken man, and equilibration may be so much disturbed that support becomes necessary. Yet the movements of the lower limbs as the patient lies on his back, or when fully

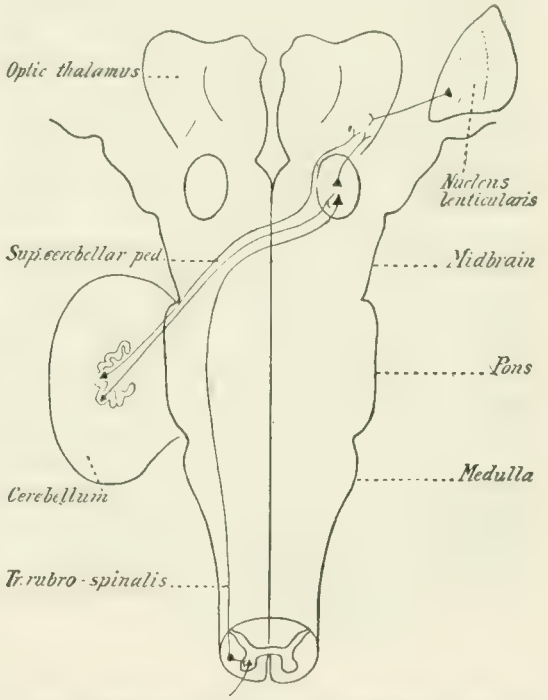


Fig. 1294.—Illustrating the Centers and Paths, Lesions of Which Cause Tremor and Involuntary Movements. (Holmes.)

supported, are not in equal degree ataxic; the difficulty in maintaining equilibrium and directing locomotion is consequently due not so much to the ataxia of the legs as to a disturbance of the synergia of the muscles of the legs and trunk which is necessary for balance.

But the limbs never escape completely; the finer movements are at least awkward and slow, and often show signs of asynergia and dysmetria; Babinski's adiadochokinesia can be usually demonstrated. In certain forms of cerebellar atrophy, tremor, when the limbs are unsupported or even during motion, is a promi-

nent symptom, and oscillation of the head is common in the severer cases. When the patient stands erect, or even as he sits more or less unsupported, the body may be seen to sway about irregularly. Occasionally even the movements of the face, both volitional and expressional, are ataxic and dysmetric; while speech is even more frequently affected than in acute cerebellar disease, being slow and drawling, or explosive and scanning. Nystagmus is, on the other hand, not so common or so characteristic. Vertigo is a frequent symptom; it is usually of the indefinite variety, and not accompanied by any definite sense of rotation of self or of external objects. In the sudden attacks the patient may lose equilibrium and if without support fall.

Hypotonia, too, has been frequently described as a symptom of chronic cerebellar disease, but though it is undoubtedly as a rule present, it is in my experience rarely marked or prominent. The affected limbs are usually feeble in relation to their muscular development, but local palsies or pareses do not occur.

The reflexes are unaltered, unless their normal state be disturbed by associated lesions of other parts; and sensation remains unaffected.

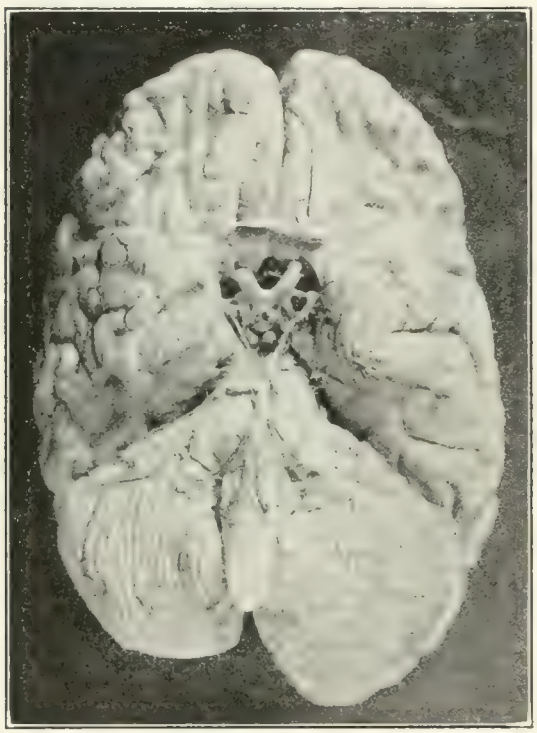


Fig. 1295.—Partial Atrophy of a Lateral Half of the Cerebellum.

2. Lesions of the Cerebellum Itself.—Of these the most important are ageneses or aplasias, scleroses or atrophies, hemorrhage, softening, inflammation, abscesses, and tumors.

Aplasia of the Cerebellum.—The number of these congenital defects is very large, and their study comprises a problem of which the solution may be aided materially by the later researches in localization. The conditions vary greatly: there may be a total absence of the cerebellum; absence of the lateral (in old sense) lobes, of the vermis, unilateral loss, irregular defects, and general smallness of the cerebellum and cerebrum. Mingazzini has attempted to group the symptoms, but with our present knowledge of the subject a consistent arrangement has not been found possible. The following groups may be recognised clearly:

A. Pure Unilateral Ageneses and Atrophies.
B. Pure Bilateral Ageneses and Atrophies.
C. Cerebellar Atrophies associated with
   (*a*) Disease of the Cerebrum.
   (*b*) Disease of the Spinal Cord.

A. *Unilateral Ageneses and Atrophies.*—There may be absence of a lateral (in old sense) lobe without the presence of symptoms which can be elicited by the modes of testing which we at present possess, though not many cases have been tested by the later methods which have been developed, and a larger experience may show better results. Some slight motor signs such as slowing of the gait has been observed where the atrophy involves a part of the vermis; whereas epileptiform convulsions or retropulsion may be associated with unilateral atrophy when the superficies of the affected hemisphere is affected. (Fig. 1295.)

B. *Pure Bilateral Agenesis.*—Here the symptoms most commonly observed are difficulties in standing and walking. In the mild grades the stand is wabbly, the feet placed far apart, but walking is possible with assistance. Where, however, a high grade of atrophy or aplasia exists the patient is absolutely unable to stand, and sometimes is even unable to sit up. Where walking is possible, the gait shows the classical drunken stagger. The lack of correlation in the trunk and lower extremities is very marked, and is also to be noted in the upper extremities where tremors and ataxias are also present. Other symptoms are hypotonus, muscular weakness, slow, irregular, hesitating, or explosive speech (these latter are also seen in bilateral atrophies). Adiadochokinesia is usually added to the other symptoms, and nystagmus is also sometimes present. The knee jerks are usually normal, and may be slightly exaggerated even in the presence of hypotonus.

C. *Combined Aplasia of the Cerebellum and Brain.*—This was described by Holmes (*Brain*, 1907) as congenital smallness of the central nervous system with cerebellar symptoms. Individuals suffering from these defects are idiotic and imbecile and show symptoms similar to those seen in cases of bilateral agenesis. In a case reported by Combette, there was total absence of the cerebellum. The patient was imbecile, and was subject from birth to epileptic attacks. Though he was able to walk, he often fell, and there was great weakness of the muscles of the neck and extremities.

A number of conditions may be grouped under this head, and some of the so-called hereditary cerebellar ataxias described by Marie are best included in this group. Irregular staggering gait, Romberg sign, disorder of speech, nystagmus, ataxias of limbs are the chief symptoms shown by these patients with small cerebellums though apparently intact tracts in cerebellum and cord.

Olivoponto-cerebellar Atrophy.—This type of disorder which Mingazzini included among the combined aplasias shows a definite syndrome, and is described by Thomas under a separate heading. The anatomical features are atrophy of the cerebellar cortex, of the bulbar olive, and of the gray matter of the pons, total degeneration of the middle cerebellar peduncles, partial degeneration of the inferior cerebellar peduncles, and a relative integrity of the cerebellar nuclei. The usual clinical picture shows irregular intention tremor, scanning speech, nystagmus, absence of Romberg, and great defect of equilibration in standing and walking with characteristically drunken gait. The disturbance which usually appears at an advanced age, and progresses slowly, is not necessarily either familial, hereditary, or congenital.

Cerebellum and Cord Atrophies or Aplasias.—Here we find a group of very varied pictures, according to the degree of lesion in the cerebellum and the cord.

Where the lesion is greatest in the cord, we see chiefly ataxias of the upper and lower extremities, of the facial, ocular, head, laryngeal, and pharyngeal muscles, and cerebellar reeling with the Romberg sign; while later on palsies and contraction with exaggerated tendon phenomenon appear. Where the defect is greatest in the spinocerebellar tracts with normal or only small cerebellum the patients chiefly show staggering gait, scanning explosive slow speech, nystagmoid jerkings of the eyes, muscular cramps, fatigability of the muscles, normal or exaggerated knee jerks.

Some of Marie's cerebellar ataxias should be included in this group. It has been claimed by some authors that Friedreich's disease should also be included, but recent studies do not bear out this contention.

Primary Parenchymatous Degeneration.—Most of the cases of this condition, which Holmes has described, show familial characteristics. It sets in as a rule about middle life, and the progress is slow. Staggering or reeling gait is one of the first symptoms to show itself; then comes incoordination of the upper extremities, to be followed by hesitancy, scanning or explosive articulation, nystagmus, and tremor of the head and limbs. There is no clonus, and no Babinski; the sphincters are intact, and the psyche remains normal.

Hemorrhage of the Cerebellum.—This disturbance is very rare. Operative interference as a rule is useless. The symptoms vary according to the size and location of the hemorrhage. Parts of the dentate nuclei are often affected through the frequent involvement of the superior cerebellar artery. Possible extension into the fourth ventricle should not be overlooked.

The usual picture is that of marked vertigo, recurring on attempts to move, and usually persistent in non-fatal cases, cerebellar gait, nystagmus on lateral movements, and forced position of the head, depending on lateral movements. Onset of the symptoms

Fig. 1296.—Hemorrhage into the Cerebellum. (Larkin.)

is usually sudden, or preceded by pain in the back of the head with slight giddiness or forced position of the head.

The patient whose cerebellum is figured here (Fig. 1296) felt dizzy, went to the drug store with a drunken, reeling gait, and died suddenly without other signs observable.

Cysts of the Cerebellum.—Differential diagnosis of cysts and cystic tumors is very difficult as the symptoms are practically identical, the operative outlook in the case of cysts being much better than in that of tumor. Together they form a small proportion (five to ten per cent.) of tumor formation in the cerebellum.

Cerebellar Tumors.—Before discussing tumors of the cerebellum proper and their symptomatology, a word may be said regarding the question of cerebellar localization. The researches in comparative anatomy by Bolk and others have established with a fair degree of certainty the existence of definite localizations in the cortex with reference to sensory representations, and in the intrinsic nuclei with reference to motor representations from different portions of the body.

With regard to sensory representations Horsley, in a study, published in *Brain*, 1909, on the terminations in Gowers' tract particularly, concludes that there is no evidence of differentiation of the cerebellar cortex into localized receiving stations for ascending impressions (muscular, arthritic) from the arm, trunk, or leg muscles, joints, etc., respectively, holding that the work done by Bolk and others did not make sufficient allowance for the possibility of lesions of the adjacent nuclei.

However true this may be of the distribution in Gowers' tract, it does not hold true of the distribution in the olivocerebellar tract, for Stewart and Holmes have shown that fibers from certain portions of the inferior olives pass to definite regions in the contralateral cerebellar cortex (*Brain*, 1908). The raison d'être of these olivocerebellar paths is not yet exactly known. Up to the present time, exact knowledge is absolutely lacking as to localization for other receptor paths (chemical, etc.).

Holmes in an important contribution to the subject of cerebellar localization (White and Jelliffe, Modern Treatment of Nervous and Mental Diseases, 1913), write that if the symptoms of lesions in different portions of the cerebellum differ it is necessary to assume the separate localization of certain functions in the cerebellum. What evidence is there of functional localization in this organ? This question can be considered from different points of view—in the first place one might ask if any of the essential symptoms of cerebellar disease, as ataxia or atonia, results from a lesion of one region of the cerebellum only; or secondly, if any portion of the cerebellum is concerned more or less exclusively with the control of any group of muscles, or even of any part of the body, as of an arm or of the eyes. In this discussion it would be desirable to consider the cortex and the central nuclei separately, but as yet so little is known of the functions of the latter that they cannot be profitably discussed. For years Luciani's view, that the cerebellum is a functionally homogeneous organ and that all parts of the cortex are functionally equal, has held sway. It is true that many physiologists, and especially Ferrier, obtained different motor effects from the electrical stimulation of different regions of the cortex, but it was generally believed and has been now shown that these motor effects were largely, if not entirely, due to spread of the current to neighboring parts: Horsley and Clarke have proved that the cerebellar cortex is relatively inexcitable. Recent work, especially by the Dutch anatomist, Bolk, has again aroused interest in the question. From an extensive study of the comparative anatomy of the cerebellum he came to the conclusion that certain regions of this organ are developed in relation to the activities of certain parts of the body, and therefore assumed a functional correlation between them. Shortly stated, he believed that the unpaired part of the cerebellum—the vermis, controls bilaterally synergic movements, as those of the trunk, and of the limbs in gait, while each lateral lobe is the center for the control of simple and independent homolateral movements.

This view has been further elaborated by van Rynberk and others, according to one of their schemes, the muscles of the head, eyes, and larynx are represented in the anterior vermis, next in order posteriorly the muscles of the neck and the bilaterally innervated movements of the limbs, and in the posterior vermis the muscles of the trunk. By the anterior portion of the lateral lobes the unilateral movements of the upper extremities are controlled, and the lower limbs by

their posterior halves. These views have received some support from the experiments of van Rynberk, Luna, Pol, Rothmann, and others, but their results have not been sufficiently uniform to admit a general conclusion. Clinical observations in man have not yet tended to confirm this theory of strict localization of function in the cerebellum, and interesting though it may be, and possibly important for future work, we must conclude that as yet if has no clinical significance.

On the other hand, clinicians from the time of Nothnagel's observations (1876) have been inclined to ascribe considerable differences to the symptoms evoked by disease of the lateral lobes and of the vermis, and some have even asserted that recognizable symptoms are due to affection of the latter only. But though this view can certainly not be maintained there is no doubt that a lesion of the vermis generally produces more disturbance than one of equal size in the lateral lobes, and it usually shows itself more prominently in the affection of equilibrium. There seems much justification for Thomas' assertion that the vermis is especially concerned in the maintenance of those coordinations on which the equilibrium of the body depends, while the lateral lobes regulate the individual and more specialized movements of the limbs.

This view conforms with the chief anatomical connections of each part; it is the vermis that receives the afferents from the vestibulum, the organ of equilibration, and the direct spinocerebellar tracts, while the chief connection of the lateral lobes is with the fore-brain which controls and regulates the more specialized movements of the limbs.

Finally, the most important clinical application of the doctrine of cerebellar localization is that unilateral lesions of the cerebellum produce predominantly homolateral symptoms, and the more strictly unilateral a lesion is, and the less it invades the vermis, the more strictly will the symptoms be homolateral.

The occurrence of cerebellar tumors is of relative frequency, particularly in childhood and adolescence, one-third of the brain tumors seen occurring in these early years being of cerebellar origin, the order from the point of view of number being glioma, tubercle, sarcoma, and fibroma.

The most commonly noted symptoms are headache, usually severe and occipital or frontal, and likely to be confined to a sagittal plane, papilloedema, rapidly progressive optic atrophy, vomiting, vertigo, and tenderness over the occiput to percussion. Percussion should never be neglected, and the cracked-pot sound to which Oppenheim has called attention, should be carefully listened for.

The symptoms just enumerated are those which are generally found in tumors of the hemispheres with no involvement of the central tracts, or the intrinsic nuclei. It is rarely however that implication of these structures does not give rise to added symptoms, such as the classical cerebellar syndromes of gait and attitude, asynergia, ataxia, and adiadochokinesia of the same side, with hypotonia of special character already described, and motor paresis of the same side. The eye deviations and nystagmus already noted are usually present. The nystagmus is apt to be pronounced only on looking to the affected side and is usually slower and coarser than the nystagmus of labyrinthine origin or of involvement of the vestibular tracts. But as these tracts are likely to be affected, too fine a distinction in the character of the nystagmus is useless. The abdominal reflexes, as a rule, are not modified. Arm and leg tendon reflexes are not lost, nor are they markedly exaggerated unless the pyramidal tracts are influenced by pressure, and there is absence of the pyramidal tract involvement signs of Babinski, Oppenheim, Schaefer, Chaddock, and Remak.

With the growth of the tumor, other symptoms, such as eye palsies, signs of involvement of the pyramidal tract, and of the cranial nerves from the fifth to the twelth are added to the picture. These symptoms all show on the other side of the body. They are due to encroachment or pressure upon contiguous structures. The two lower branches of the facial are involved, the tongue protrudes to the paralyzed side but is without atrophy or reaction of degeneration. Sometimes the medulla is pressed upon and in this case all the branches of the facial are involved and atrophy of the tongue is present. There may be trigeminus involvement, in which case homolateral anesthesia will be present, or possibly homolateral affection of the ears such as deafness or buzzing. Homolateral pain to pressure in the mastoid may be an aid to diagnosis. As pressure increases, unilateral signs are likely to be succeeded by bilateral signs with dysarthria, dysphagia, continued vomiting, and finally cardiac and respiratory involvement. Lumbar puncture may be of great assistance in differentiating hydrocephalus or meningitis serosa. When the case is not seen until the last stages, recourse must be had to the history.

The more detailed symptomatology from the work of Holmes (*loc. cit.*) is in brief as follows:

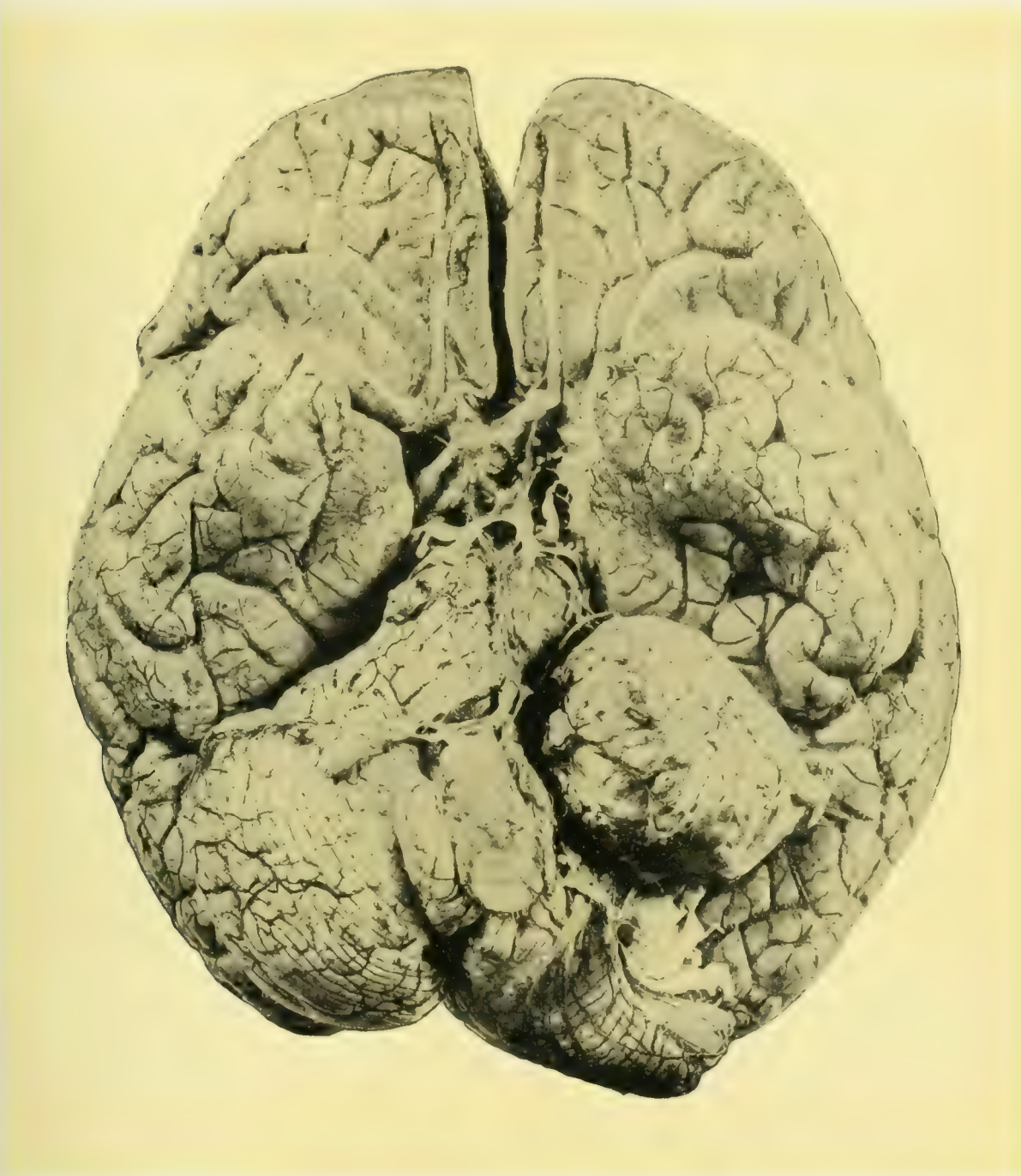
As a rule, the more rapid the evolution of the tumor, and the more destructive it is, the more pronounced and definite are the symptoms. But it is also in such cases that the physical signs are often obscured or complicated by the indirect pressure which the tumor exerts on portions of the cerebellum it does not involve, or on neighboring organs in the brain-stem; for instance a tumor that involves only one lateral lobe of the cerebellum may disturb the functions of the vermis, or even those of the opposite lateral lobe, as well as those of the pons and medulla.

Ataxia.—Ataxia is usually the most prominent symptom; when the tumor lies in one lateral lobe this is exclusively or predominantly present in the homolateral limbs. If the vermis is involved it is bilateral and as a rule relatively greater. It is more marked when the lesion involves one of the peduncles, especially the inferior, than when it is superficial. If the superior peduncle be affected the disturbance of movement frequently approximates to the intention-tremor type rather than to the characteristic ataxia. Apart from this it cannot be said that the ataxia is a guide to the exact site of the lesion. As in all acute lesions the disturbance of equilibrium in gait is more prominent than the ataxia of the simpler movements; in unilateral tumors the patient reels and staggers to the side of the lesion, but this rule is not absolute as the reeling occasionally is chiefly toward the sound side; this seems to be due mainly to a volitional attempt of the patient to compensate the defects the lesion produces by shifting his center of gravity as far as possible toward the healthy side. In tumors of the vermis or those of bilateral extension, gait is usually much more impaired. Tumors in the anterior portion of the cerebellum usually produce less disturbance of coordination and equilibrium than those situated posteriorly.

Frequently unilateral tumors produce a more or less characteristic attitude of the head; it is generally rotated with the chin toward the healthy side and at the same time flexed toward the affected side so that the occiput approaches the shoulder on the side of the tumor. Hypotonia and paresis seem to be more pronounced when the inferior peduncle and the central nuclei are involved.

Nystagmus.—Nystagmus is one of the most valuable symptoms; it is usually apparent only on lateral movement of the eyes, and the conjugate excursions are slower, more forcible, and wider in range, on movement toward the affected than to the healthy side. Nystagmus on vertical movements of the eyes suggests a lesion in the anterior portion of the cerebellum and is thus a valuable localizing symptom.

Vertigo.—Vertigo is certainly much more common and of a more definite type in lesions of the postero-



TUMOR OF THE CEREBELLUM

inferior portions of the cerebellum than elsewhere; this is probably due to the fact that it results chiefly from disturbance of the vestibular connections. True vertigo with a distinct sense of rotation of self and of surrounding objects is in Holmes' experience rare with tumors in other parts of the cerebellum. Despite the lack of confirmation by other clinicians Holmes is convinced of the importance of the directions of the apparent rotations as a differential sign in the diagnosis of unilateral intracerebellar and pontocerebellar tumors; in the former the movement of both self and the external world seems to be from the affected toward the healthy side, but in the latter class, self seems to rotate toward the affected side, but external objects from the affected to the normal side.

But it is largely on the accessory symptoms that one must rely in the localization of the site of the lesion. In this respect ocular palsies are important. Disease limited to the cerebellum cannot produce directly paralysis of any ocular muscle, or palsy of any movement; in cases of cerebellar tumor, however, palsies are not infrequent for they result either from a general rise of intracranial pressure, or from compression of those parts of the brain-stem that contain the ocular nuclei. Isolated palsy of one external rectus is most commonly due to a general rise of intracranial pressure, and, as is well known, frequently occurs with this condition no matter what its cause is. It is consequently of no localizing value. An external rectus palsy may be, however, due to compression of the sixth nerve by a tumor of the cerebellopontine angle. A conjugate weakness of lateral movement of the eyes, on the other hand, results from compression of the homolateral sixth nerve nucleus by a tumor in the posteroinferior portion of the cerebellum, or possibly from interference with a supranuclear center for conjugate movement, in or near Deiters' nucleus. Vertical movements are very rarely affected by intracerebellar tumors, but occasionally a weakness of upward movement results from the compression of the midbrain by a tumor that lies far forward in the cerebellum. The pupillary reactions are not disturbed.

The so-called "skew-deviation" of the eyes, the eye on the side of the lesion being directed downward and inward, the opposite outward and slightly upward, seems to occur chiefly with acute lesions that involve the cerebellum in the region of entrance of the middle and inferior peduncles.

A slight inferior neuronic weakness of one side of the face is occasionally observed when a large tumor lies low in the cerebellum and compresses the pons; a greater weakness is usually due to extension of the tumor into the pons, or to direct compression of the facial nerve by a tumor of the cerebellopontine angle. When a tumor lies far laterally in the cerebellum the trigeminal nerve may be compressed, but as a rule only its sensory portion suffers; this usually produces only pain or paresthesia on the same side of the face, actual sensory loss being rare. The corneal reflex, however, is often lost very early. Intracerebellar tumors and tumors involving the pons, however, frequently produce complete or considerable anesthesia in the distribution of the trigeminal nerve, with weakness or paralysis of the muscles innervated by its motor root. This is consequently an important sign in the differential diagnosis of these different conditions.

Disturbances of hearing are very important; while more or less complete unilateral nerve deafness is the rule in extracerebellar tumors, any degree of deafness is rare with intracerebellar growths. Tinnitus, on the other hand, is common in cerebellar tumors, but it is rarely so persistent or severe as with tumors of the cerebellopontine angle.

Affection of the functions of the glossopharyngeal, vagus, and hypoglossal nerves is very exceptional in intracerebellar disease, but some weakness of the same side of the palate is not uncommon with tumors of the cerebellopontine angle.

Cerebellar Abscesses.—These are not infrequently seen and may vary in size from that of a pea to an apple. Their development may be either acute or chronic. They usually arise from middle ear infection, by way either of the temporal lobe or of the mastoid, and may result from wounds or trauma, the latter of which may have happened at a long prior date. Ulcerative endocarditis, abscess of the lungs, or infectious thrombus may occasionally prove to be the exciting cause.

The characteristic symptoms are many. Of the special cerebellar symptoms ataxia, nystagmus, and rotatory vertigo are to be noted; the vertigo being made worse and vomiting induced by movement of the body (Bruns' sign). Of the other characteristic symptoms headache, generally occipital, and radiating into the neck region, with marked stiffness of the neck, is of special importance. This headache may resemble that of cerebrospinal meningitis. Nausea, vomiting, stupor, general unrest may be present, as also fever; but it is to be borne in mind that many cerebellar abscesses run for months without causing fever. Although not constant signs, hemiparesis and hemiasynergia are usually present on the same side as the lesion. Atrophy is not infrequently present in larger abscesses, and papilledema caused by pressure produced by increase in the size of the abscess may increase the difficulty of differentiating from tumor.

Actual puncture by special aspiration needle is advisable to clear up the diagnosis in complicated cases. Lumbar puncture should be resorted to, to exclude meningitis.

Associated Posterior Fossa Complications.—*Occipital Lobes.*—A foreign body growing within or upon the cerebellum may press anterosuperiorly upon the occipital lobes, causing hemianopsia.

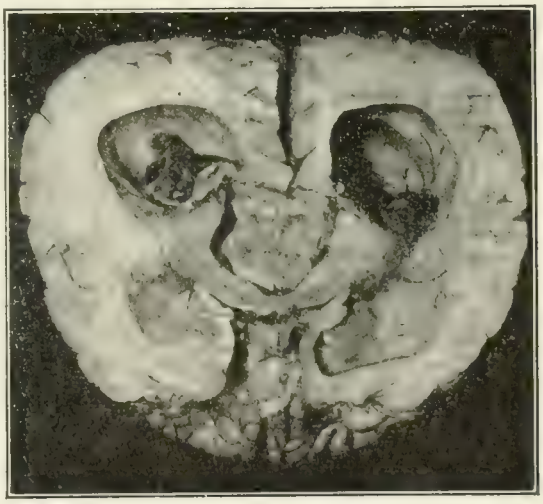


Fig. 1297.—Teratoma of the Pineal Gland compressing the Corpora Quadrigemina, Causing Nothnagel's Syndrome plus Marburg's Adiposogenital Syndrome—the Pineal Syndrome. (Bailey and Jelliffe.)

Corpora Quadrigemina.—Symptoms of a tumor of the corpora quadrigemina are primarily ocular palsies of a nuclear character, first on one side and then on the other. The trochlear is less often involved than the abducens and oculomotor. Loss of conjugate deviation of the eyes is frequent and there will probably be paralysis of accommodation or changes in the pupils. If the lateral geniculate be pressed upon there

will be amblyopia without papilledema. Deafness may be present, caused by involvement of the posterior corpus, and of the middle geniculate. Care should be taken in differentiating pineal tumors which produce a picture almost exactly the same. (Fig. 1297.)

Cerebral Peduncles.—Tumors of the cerebral peduncles are productive of varied symptoms. If the lesion be severe, alternate hemiplegia and oculomotor palsy (Weber-Gubler) will probably result. The appearance of Benedict's syndrome—oculomotor palsy with tremor of the opposite side—speaks of pressure of less severity; whereas crossed anesthesia and ataxia point to impairment of the lemniscus. (Fig. 1298.)

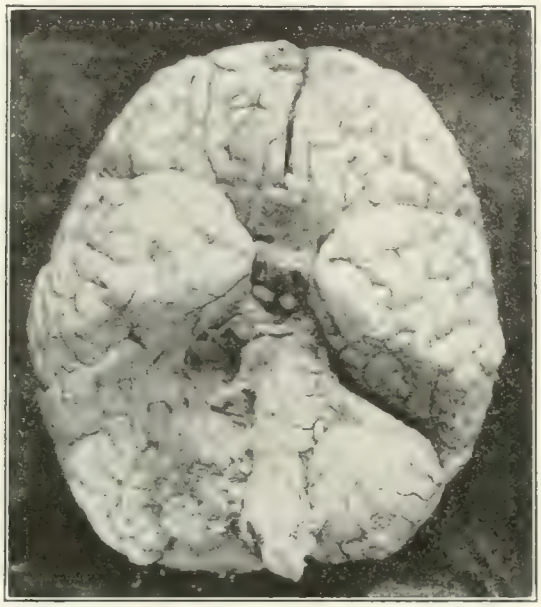


Fig. 1298.—Tumor of the Cerebellum with Destruction of the Right Lobe and Middle Cerebellar Peduncle. (Jelliffe and Larkin.)

Pons.—In tumor of the pons the picture is a very complex one. Crossed hemiplegia with facial palsy (Millard) and reaction of degeneration is one of the chief symptoms. When the abducens nucleus is involved, conjugate deviation to the side opposite to the lesion is the rule, but these conjugate palsies are more likely to arise from tumors within the pons. Crossed hemiplegia and abducens palsy generally point to hypoglossal involvement. Homolateral facial palsy without reaction of degeneration is sometimes seen. Crossed hemiplegia and trigeminus involvement and also alternate hemiplegias may be found occasionally. Defect of hearing is caused in the latter case by destruction of the intrapontine fibers of the cochlearis, or by pressure on the tuberculum acusticum.

Tumor of the Fourth Ventricle.—Tumors of the fourth ventricle usually take the form of glioma, sarcoma, carcinoma, or psammoma, and by reason of pressure on the medulla and pons give rise to cerebellar symptoms which make it advisable to consider them in this place. Marked hydrocephalus with advancing stupor and confusion are nearly always present, and cysticerus may also be found. Alternating periodicity of headache, nausea, vomiting, vertigo, changes in pulse and breathing (with remission of all these symptoms) have been noted by Bruns; the vertigo and vomiting being caused by changes in the position of the head, whereas sudden movement of the head may cause immediate unconsciousness. Other signs are cerebellar ataxia, mild nystagmus and occasionally diplopia. (Fig. 1299.)

Care must be taken in differentiatingthese tumors from those of the frontal lobes, the parietal lobes, or the optic thalamus, for which they may be mistaken in presence of a few signs only.

In tumors of the *frontal lobes* (frontocerebellar paths) careful examination by the Ziehen, Sommer, and Kraepelin methods will usually show special intelligence defects. Skew deviations and hypotonia are not found in these tumors. The conjugate deviations are not paralytic but irritative; the speech disturbance usually takes the form of ataxic aphasia; hemiparesis, if present, is crossed and shows spastic phenomena, and the tremor is likely to be marked by fineness and rapidity. Anosmia, apraxia, and aphasia may be present. Witzelsucht is a not infrequent phenomenon which, when combined with the peculiar gait should not be confused with inebriety.

Partetal lobe disease (implications of central sensory components) obtrudes difficulties but rarely, while disorders of the optic thalamus should be excluded by reason of the characteristic sensory disturbances and central pains by which they are accompanied.

Cerebellopontine Angle Tumors.—These should be included in a discussion of cerebellar tumors, by reason of the symptoms of cerebellar pressure, and of vestibular involvement. There are two main types: those of the pia of the cerebellum, and those growing on or about the eighth nerve. They usually take the form of fibromata, myxomata, or sarcomata.

The symptoms vary according to the degree of pressure upon the pons and middle cerebellar peduncle. Buzzing and deafness, caused by the early involvement of the eighth nerve, soon appear. The typical gait, the ataxia, homolateral paresis, and hypotonus are caused by pressure on the cerebellum, whereas pressure on the pyramidal tracts may and usually does produce a contralateral paresis giving the usual signs

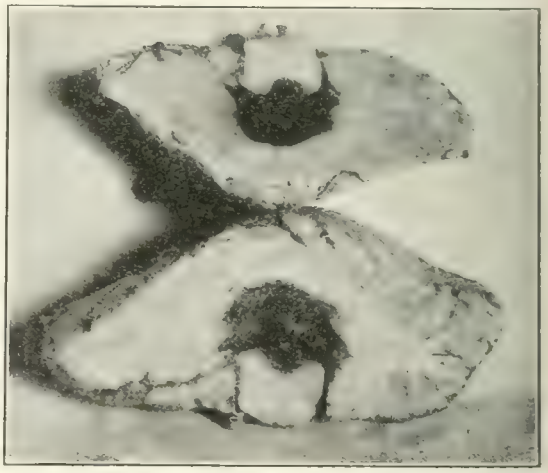


Fig. 1299.—Sarcoma of the Fourth Ventricle.

of a pyramidal tract involvement. Ptosis may be present. Facial palsy is a usual accompaniment, and corneal anesthesia to trigeminal pain, caused by pressure upon the fifth nerve, is of frequent occurrence. Homolateral static tremor and a sense of subjective rotation toward the side of the lesion are frequent.

Treatment of Cerebellar Tumors.—Generalization on the question of treatment is useless. No two cases act in exactly the same way, and treatment must be in accordance with symptoms and localization. Antisyphilitic treatment is the proper mode of attack on small gummata. Operation for cysts usually shows good results, and with greater knowl-

edge of localization, and better modes of procedure the results of operative interference in cases of abscess and tumors are improving.

Accurate localization is therefore the first essential, and it is perhaps more important in the cerebellum than elsewhere in the nervous system, as owing to the proximity of the delicate vital centers in the bulb, it is necessary to limit exploratory measures as much as possible.

It must not be understood, however, writes Holmes in his study previously referred to, that surgical intervention is to be recommended immediately on the diagnosis of cerebellar tumors. With tuberculous lesions, for instance, the danger of the dissemination of the bacillus is great; and, on the other hand, many tuberculomas cease to grow and become latent, their symptoms disappearing or diminishing as fully as could be expected after their removal and the further injury to the cerebellum the surgeon must produce in the operation. A further reason against operation if it can be avoided is the fact that tuberculous tumors are frequently multiple. Holmes speaks of patients in whom years ago the almost certain diagnosis of cerebellar tumor was made, and who now present few or no symptoms of it. Too often, unhappily, the rapid progress of the case and a threatened failure of vision from optic neuritis force the physician's hand.

If a gumma is probable vigorous antisyphilitic treatment should be adopted in the first place. Injections of salvarsan should be tried, but should be followed by mercurial inunctions alternated with large doses of iodides; the general experience at present is that salvarsan has but little influence on gummata when they are already developed. Apart from the greater safety of medicinal over the surgical treatment of gummata it must be remembered that these are frequently associated with a considerable chronic syphilitic meningitis which is not amenable to surgery.

Abscesses usually demand immediate surgical measures, but if their course is not very acute it is often advisable to wait, in the hope that they may become encapsuled and until the virulence of the infection diminishes, as otherwise the danger of the development of a general septic meningitis is great.

Simple and hydatid cysts of the cerebellum are the most favorable for surgical treatment; a considerable proportion of the successful operations have been in this class of case. When the tumor is a glioma unhappily only operation can give relief, and yet the proportion of cases in which the relief is at all permanent must be very small, as complete extirpation is rarely feasible, and the danger of recurrence is consequently great.

The various forms of extracerebellar and lateral recess tumors can be dealt with only by the surgeon, and as they are usually benign the results may be exceedingly good; the danger of the operation to life is, however, great.

Holmes and Stewart published the records of 11 cases of intracerebellar tumor which were operated on, and 10 cases of extracerebellar tumor. In the former group 5 cases died soon after the operation, 3 at least died after the paper was published, from recurrence of a glioma in 1 case, with tuberculous meningitis in another, while in the third death was probably independent of the cerebellar disease. Two cases of simple cyst survive, and possibly 1 after the partial removal of a glioma. Of the 10 extracerebellar tumors 7 patients died immediately or soon after the operation, 1 several months later with a tumor on the opposite side, while 2 survive.

Of 25 of Oppenheim's cases which were operated on 3 recovered, 3 improved, while the others died. In 31 of the cases collected by Duret death occurred immediately or within some days after the operation; in 9 others death occurred later; 8 improved, while 5 recovered. Cushing's results have been much more favorable; of 35 operations 3 proved fatal, in 2 cases the tumor was inoperable, in 17 only decompressive operations were attempted, while there were 13 successful cases of tumor extirpations or cyst removals.

Pascalis has recently collected statistics on the operative treatment of extracerebellar or pontocerebellar tumors. Of 11 cases in which only a decompression was attempted 3 died, and in 7 some improvement of the symptoms occurred; while in 101 cases in which removal was attempted 72 deaths occurred.

The promise of surgical intervention is thus not overfavorable, but with the increase of accuracy in diagnosis, the more careful selection of cases, and the improvement which experience must evolve in surgical technique, the results of the future will certainly be better. Further, the fact must be taken into consideration that the majority of cases of cerebellar tumor must, if unrelieved, progress to a fatal termination and that consequently operation often offers the only chance of recovery. (Consult the article by Halstead on "Surgery of the Nervous System," in Modern Treatment of Nervous and Mental Diseases, vol. ii., by White and Jelliffe).

But if an attempted removal of the tumor offers only such a poor chance of recovery it must be remembered that decompression alone often prolongs life and leads to a remarkable diminution of the symptoms. Life has been prolonged for months, and even for more than a year in relative comfort. Experience shows that the most successful operation is bilateral occipital decompression by Cushing's method, in which a large portion of the skull is removed on both sides.

SMITH ELY JELLIFFE.

Cerebellum, Physiology of.—See under *Brain*.

Cerebral Hemorrhage.—Hemorrhage into the cranial cavity may occur in a variety of forms, but by far the most frequent is that of a hemorrhage into the substance or structure of the brain itself. Commonly this hemorrhage is single and its chief site of election is in the basal ganglia, involving portions of the adjacent internal capsule and resulting in hemiplegia. The preponderance of this site is reflected in the common association of the terms, stroke of apoplexy and stroke of paralysis, and it was this that led to Charcot's characterization of the lenticulostriate artery as the artery of cerebral hemorrhage. This location is, however, while much the most frequent, by no means the sole site, as single large hemorrhages are encountered in practically all portions of the brain. Hemorrhages also occur beneath the membranes of the brain, *i.e.* subdural, without involvement of the cerebral structures, except secondarily by pressure; and occasionally a hemorrhage into the ventricles is found whose source is apparently one of the vessels of the ventricles, and not from the breaking through of a hemorrhage in the brain substance. The majority of ventricular hemorrhages are, however, the result of rupture into the cavities of hemorrhages in the brain substance. In the case of meningeal hemorrhages, the relation of the pia to the clot will often serve as a guide to the postmortem determination of the source. When the hemorrhage is from one of the meningeal vessels, the clot is found beneath the dura but the pia is pressed down away from the clot and not ruptured. In case the hemorrhage takes origin from vessels of the cerebral substance, laceration of the brain substance is usually evident, and the extravasation is seen spreading out beneath the pia over the convolution. The pia may be ruptured, but a considerable amount of blood will still be found to have spread out beneath it. Still another type of intracranial hemorrhage is found in chronic internal hemorrhagic pachymeningitis, in which recurring hemorrhages of comparatively small volume take place from the dural vessels with

subsequent partial absorption or organization, giving a lamellate appearance to the clot. The term pachymeningitis applied to this type of extravasation is considered by some a misnomer, in that they are hemorrhagic rather than inflammatory reactions. They are rather frequently found in the cases coming to autopsy in hospitals for the insane, and their association with cerebral atrophy is sufficiently constant to suggest an etiological relation, *i.e.* as though the reduction of cerebral volume rendered more easy subdural extravasations. Bevan Lewis recorded this finding eighty-one times in a series of 1,565 autopsies of the insane of all types, and thirty times in a series of 242 autopsies in cases of general paralysis. The amount and volume of the hemorrhage is very variable. In typical cases, that portion of the dura over the dome suffers most, but the blood may be spread over all of one or both hemispheres. Traces of partial organization or evidences of clots of varying ages and in various stages of disintegration usually serve to distinguish this type from the simple subdural hemorrhage. Many times this is impossible, and it is probable that there is no distinct line of division between the two.

Multiple miliary or punctate hemorrhages are found in association with marasmus in children, and occasionally in the adult. Massive hemorrhage of the brain is usually the result of venous thrombosis. Multiple hemorrhagic foci associated with softening make up the postmortem picture of acute red softening or acute hemorrhagic encephalitis, which, as its name indicates, is a disease of inflammatory nature, associated frequently with brain infections by the pyogenic staphylococci and the pneumococcus.

Cerebral hemorrhage is usually stated to be more frequent in men than women, one ratio given is that of 7 to 4. Von Monakow questions this statement, finding in the Canton of Zurich no difference between the sexes, and explains the usual findings on the ground that the men are more apt to find their way into hospitals than the women.

The following table shows the proportions according to sex as found by several authors.

	Male.	Female.
Gintrac	407 cases	299 cases
Fabret	1,660 cases	637 cases
Kelnack and Bytnell	77.1 per cent.	22.9 per cent.
Von Monakow	No noteworthy difference.	

Von Monakow calls attention to the fact that statistics compiled from cases without postmortem examination are unreliable, as many cases of embolism, thrombosis, encephalomalacia, encephalitis, etc., would find their way into such records.

Age bears an important relation to the occurrence of cerebral hemorrhage. The following table taken from Lewandowsky's Handbuch der Neurologie, gives the results of Gintrac's analysis of a series of 653 cases showing their distribution by decades and Gower's findings of the frequence of occurrence in 1,000 persons of each decade.

Age.	Percentage distribution of cases.	Percentage occurrence in 1,000 persons.
1–10	2.3	0.8
11–20	3.1	1.3
21–30	6.0	2.6
31–40	10.8	5.2
41–50	15.1	8.3
51–60	19.8	13.5
61–70	24.4	22.4
71–80	17.2	32.4
81–90	1.8	14.0

In both tables, the figures show the great preponderance of occurrence after the age of forty to fifty years and at the same time they demonstrate the rather sharp drop in the ninth decade. In such tables again, especially in the cases occurring before the fourth decade, one must make allowance for the inclusion of many cases of cerebral syphilis or syphilitic endarteritis, embolism and thrombosis, and the after-results of trauma.

Etiology.—In consideration of the generally accepted etiological factors, it may be well first to dismiss some of the hemorrhagic conditions mentioned above before confining ourselves to the more common types. Acute red softening is an acute type of encephalitis and need not be considered here. The majority of the massive hemorrhages of the brain are the result of thrombosis of the venous channels, and the miliary hemorrhages are found in association with marantic thrombi. These two conditions have been described in the article on *Brain, Circulatory Disturbances of the*, and need no further notice here. The leakage of blood in chronic internal hemorrhagic pachymeningitis is as a rule small and this together with its recurrence, which results in the building of lamellate layers of clot in varying stages of alteration and organization, serve to distinguish it from the gross type of subdural hemorrhage. One occasionally meets, however, at the autopsy table, a large hemorrhage associated with undoubted signs of precursors, *i.e.* partly organized clot sheets, etc. This suggests the possible intimate relation between the single spontaneous subdural hemorrhage and the pachymeningitic type. It is only necessary to presuppose that the difference in the two is chiefly that of a single lesion in a large vessel and multiple lesions in smaller ones. This conception is strengthened by the fact that in the larger hemorrhages, the ruptured vessel can be found often with some ease, while in the recurrent variety the search is an arduous and generally a futile one.

Chronic internal hemorrhagic pachymeningitis finds its most frequent association with general paresis and with cases in which marked cerebral arteriosclerosis is evidenced by advanced cortical atrophy, cysts of softening in the brain, etc., and while the single large subdural hemorrhage may also be found in these conditions, its occasional spontaneous occurrence groups it more intimately with the classical apoplectic type of cerebral hemorrhage. Trauma, especially that resulting in fracture of the skull, is one of the causes of subdural hemorrhage by laceration of one of the meningeal vessels.

The etiological factors of spontaneous cerebral hemorrhage have been the subject of a statistical study by Lowenfeld on the literature preceding the year of publication, 1886. He has analyzed this material in relation to (1) arteriosclerosis of the basal vessels; (2) organic heart lesions, especially hypertrophy; (3) chronic nephritis; (4) alcohol, lead poisoning, rheumatism, and syphilis; (5) the so-called apoplectic constitution; (6) heredity.

He concludes that *arteriosclerosis* plays little direct part in the etiology of cerebral hemorrhage. In subjects of sixty years of age and over, approximately eighty-five per cent. show sclerotic changes of greater or less degree in the great vessels of the brain, while the occurrence of cerebral hemorrhage is not of comparable frequency. Again there is a marked drop in the number of cases of hemorrhage occurring in the ninth decade, while arteriosclerosis appears in advancing ratio. When contrasting series of similar age with regard to the occurrence of basal arteriosclerosis, those who have suffered with cerebral hemorrhage do not form a noticeably larger group than those who have succumbed to some other disease. He also noted that the majority of cerebral hemorrhages occur from relatively small vessels, and that, as a rule, the

brunt of the sclerotic and atheromatous processes is borne by the larger arterial trunks. He found that in a series of fifty-six cases of hemorrhage the basal arteries were normal in sixteen, showed slight sclerosis or atheroma in eighteen and advanced atheroma in twenty-two. Similarly advanced arteriosclerosis of the aorta and other large vessels of the trunk is excluded as an etiological factor of importance.

Other observers have pointed out, however, that arteriosclerosis may play an important indirect part in the causation of cerebral hemorrhage, by reducing the elasticity of the larger trunks, so that the tension of the blood stream is transmitted with less reduction to the smaller and more delicate vessels taking origin from them.

Eulenberg came to the conclusion that *cardiac hypertrophy* was of importance from the standpoint of cerebral hemorrhage only when it was the result of chronic nephritis, arteriosclerosis, or some condition tending toward a chronic increase of the blood pressure and not in the hypertrophies which were compensatory in nature. Lowenfeld on the other hand, found that in cases of hemorrhage in the fifth decade, hypertrophy of the heart was found in seventy-five per cent. and that no apparent difference could be traced to the type of the hypertrophy. On the whole it may be considered that the part played by cardiac hypertrophy in spontaneous cerebral hemorrhage is largely a secondary one, dependent on the heightened blood pressure which is its concomitant, or possibly in some cases on a common etiological factor whose attack results not only in the organic heart lesion and consequent hypertrophy, but also in focal lesions of the vessel walls.

Chronic interstitial nephritis likewise may play an important part through the increased blood pressure which accompanies it. It is found at autopsy in a considerable number of cases of cerebral hemorrhage (twenty to thirty per cent.), but not with more frequency than in persons of similar age dying of other diseases. Multiple small hemorrhages seem more prone to accompany chronic nephritis than single large ones.

No association has been established between *alcoholism*, *lead poisoning*, and other similar toxic conditions and cerebral hemorrhage except the indirect bearing they may have in the production of arteriosclerosis, cardiac hypertrophy, and increased blood pressure. Rheumatism has similarly not been directly implicated, but the association of endocardial lesions with this disease is of interest here, suggesting the possibility of foci of damage to the arterial endothelium as well as that of the valves. The part played by syphilis in cerebral hemorrhage is an uncertain one which doubtless will receive some light by further researches by means of the Wassermann reaction and the newer histological measures. Hemorrhage is rare in the secondary stage of syphilis, but more frequent in the tertiary. In this class fall many of the apoplexies of comparatively young persons who show no other obvious predisposing condition. One must be careful, however, in arriving at a diagnosis of hemorrhage in these cases on account of the difficulty of differential diagnosis between hemorrhage and softening from obliterative endarteritis.

Considerable attention is drawn to the so-called *apoplectic type* or constitution which is characterized by a short thickset body, short thick neck, general corpulence, and a plethoric face. Little accurate observation is recorded of the relative frequence of occurrence of cerebral hemorrhage in this type as contrasted with others. Kirsch records cerebral hemorrhage as the cause of death in one-third of a series of cases of sudden death in persons with marked excess of fat. Gowers states that the majority of cases he has seen lacked entirely the apoplectic habitus and were thin, lank individuals, while Lowenfeld in a series of eighty-four cases found only thirty in which excess of fat was not noticeable. Von Monakow suggests that irregular life and alcoholic excesses may predispose toward fat as well as to cardiorenal and vascular disease, and that this may be the reason for the higher proportion in fat individuals. He points out that Lowenfeld's work was done in Munich where beer consumption is large and the number of well-favored individuals is greater than elsewhere.

Heredity has long been held to be a factor of importance, but its exact relationship is not as yet entirely evident. Lewandowsky calls attention to the fact that many cases in the literature of so-called hereditary apoplexy were doubtless cases of congenital syphilis. Lowenfeld states that an hereditary local defect of the cerebral vessels seems possible, but is not demonstrated. Heredity may play a part through a disposition for the establishment of some of the associated indirect etiological factors, *e.g.* arteriosclerosis, organic heart disease, chronic nephritis, etc. Familial tendencies toward hemorrhage and allied conditions have been pointed out by Raymond, Spiller, and Weisenberg, while on the other hand Gowers reports other families as exempt through several generations. Dieulafoy suggests that hemorrhage occurs at an earlier age in each succeeding generation and records a case of apoplexy in a youth of seventeen whose mother suffered a hemiplegia at forty-six, while the grandmother died of cerebral hemorrhage at an advanced age.

Among the *direct causes* of cerebral hemorrhage, one again meets a curious contradiction. It may occur during periods of rest and not infrequently during sleep. Von Monakow considers it possible that the conditions during sleep are more favorable to hemorrhage by reason of the increase of pressure in the vessels of medium size through the horizontal position and the contraction of the cortical capillaries. On the other hand severe exertion, lifting heavy weights, vomiting, and paroxysms of coughing are recorded as determining factors. Sudden reduction of cerebrospinal pressure by lumbar puncture is also mentioned.

Pathological Anatomy.—The vascular lesion most frequently associated with the classical type of cerebral hemorrhage is the miliary aneurysm. Several early writers had recorded the finding of such aneurysms, but Charcot and Bouchard called attention to their association with hemorrhage in recording them as the constant source of the bleeding in eighty-four cases. Subsequent observation by numerous authors seems to indicate that while an occasional case may be found in young persons, in which cerebral hemorrhage is associated with arteries which are apparently normal, yet in the great majority of cases, search will reveal the miliary aneurysms, generally in considerable numbers. Maceration of the brain substance in water leaves the vascular tree free for examination, and the aneurysms may be made out with ease either by the naked eye or by means of low magnification. They vary considerably in size in different cases and even in the same case. Commonly they are spherical or cylindrical enlargements of the small vessels of approximately one-half to one millimeter in diameter with a color varying with their characteristics. In some the walls are thin and the blood beneath gives them a bluish or dark red color—in others sclerosis and calcification result in thick walls of an opaque yellow or grayish-white. Similarly their consistence varies from that of a soft, easily compressible mass to that of a hard calcareous nodule.

Charcot records the finding of miliary aneurysms at all ages above twenty, but with a rapid increase about the age of forty. They are also found in considerable numbers in those of advanced years dying of other causes than cerebral hemorrhage. Charcot's

suggestion that the miliary aneurysm is a lesion sui generis, and not merely an accident of the more common forms of arterial disease, has led to considerable discussion. Charcot believed that the primary change was a periarteritis followed by a fatty degeneration of the muscle layer and that intimal changes were secondary. Zenker reports the finding of intimal changes of a sclerotic type in every case of miliary aneurysm examined, and considers them to be merely one form of expression of arteriosclerosis, and to have their origin in disease of the intima.

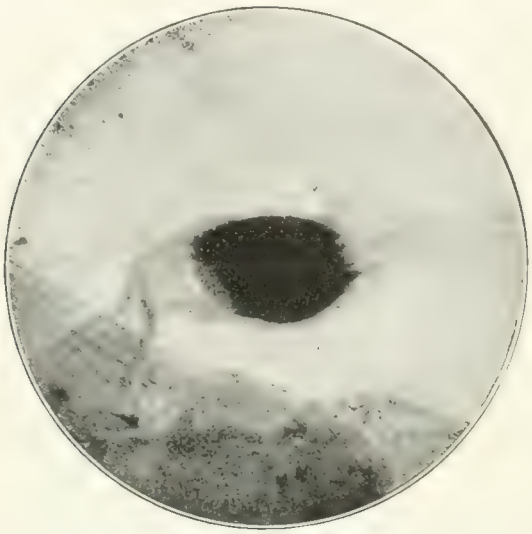


Fig. 1300.—Low Power Microphotograph of a Miliary Aneurysm. Revealed by maceration of the brain substance in a case of cerebral hemorrhage. (From the collection of the Department of Neuropathology, Harvard Medical School.)

Roth called attention to the rare occurrence of atheroma in the smaller vessels and to the fact that even when it did appear, aneurysms did not always occur. He considers a fatty change of the muscularis to be the primary disturbance, with next a stage of cylindrical widening through the degeneration of the circular muscle coat, then bulging of all three coats, and lastly a secondary compensatory thickening of the media and adventitia. Lowenfeld is in agreement with this idea and considers them as a special kind of arterial disease whose starting-point is in the muscularis. He regards the intimal changes as inconstant, and not essential and points out that they may occur in cases where there is no other demonstrable sclerosis, and, on the other hand, may be lacking in cases with very advanced sclerotic and atheromatous change. Von Monakow considers them to be the result of a periarteritis, and directly dependent on degenerative changes resultant therefrom in the muscle coat.

Care must be taken in interpreting the lesions found at the site of a hemorrhage as secondary ruptures and further bleeding may result. The pressure exerted by blood escaping at arterial pressure collapses the arterioles and capillaries of the adjacent fields, and results often in softening of brain substance, and necrosis of vessel walls so that they may give way, or allow the escape of blood cells by diapedesis under returning circulation, or by reflux from the venous system where the pressure is also abnormally high.

Vessels collapsed by the pressure at some part of their course will, nearer their source of supply, be under increased tension, and transudation gives rise to edema of the surrounding structures which Hill points out as a source of establishment of a sort of circulus vitiosus.

Larger aneurysms may occur on the cerebral vessels and give rise to extensive hemorrhage on rupture. As a rule this type spring from large vessels and their rupture is rapidly fatal. They are probably often, if not always, syphilitic in origin.

At autopsy the hemorrhage presents a variable appearance depending on its size and age. In immediately fatal cases, where the examination takes place within a short time after death, the blood may be found unclotted. Usually, however, the clot is formed and is of a dark red or almost black color, fairly firm, and mingled frequently with shreds of brain tissue. Gradually absorption of the clot begins, and the remnant passes through a series of color changes, from chocolate brown through light brown to reddish yellow. Disintegration of torn brain tissue and clot gives rise to a large amount of detritus, which gradually undergoes solution and partial removal, and at this stage, the microscope shows fragments and detritus, and blood pigments all being actively engulfed by large phagocytes. There is, however, in the brain, little or no attempt at organization of the clot, such as occurs in other parts of the body. The connective-tissue elements accompanying the blood-vessels apparently do not react to any marked extent with the production of new tissue, and the glia is not efficient in replacing any suddenly occurring large loss of tissue. There is evidence that the glia will react to a slowly advancing ischemic process, with proliferation which is abundant, but in areas of hemorrhage and softening in which the ischemia is sudden and complete, little or no replacement occurs, and a cyst is formed, in which the glia reaction is limited to a circumferential or capsular zone. In small hemorrhages, the resorption may be comparatively complete and all that remains is a small glia scar with occasionally some pigmentation of the adjacent tissues. In larger ones, after a sufficient period, a cyst is found filled with clear fluid, and with yellowish walls and at this stage it may be impossible to decide, whether the original lesion was a hemorrhage, or an area of softening. In autopsies on early cases, signs of intracerebral pressure are evident; the convolutions are flattened and markedly pale; the cerebrospinal fluid is small in amount, and frequently tne hemisphere which contains the lesion is noticeably enlarged and encroaches on the sound hemisphere, except where it is held back by the falx cerebri. The amount of pressure, and partition-like action of falx, is often beautifully indicated by the sharp line of indentation made by the lower edge of the falx on the enlarged hemisphere. The brain tissues immediately adjacent to the hemorrhage are frequently the seat of softening, which may be anemic in type, though frequently associated with punctate hemorrhages or extravasation by diapedesis.

The secondary changes taking place in the nervous tissues following hemorrhage are, of course, dependent on the site and amount of destruction. Regeneration probably does not take place in the nervous elements of the central nervous system. Allen has shown that cells in active mitosis disappear from the brain of the white rat at about the twentieth day after birth, and it is probable that in man even before birth the structural units of the brain and cord are so fully differentiated that no replacement follows destructive injury. Nerve fibers which have been cut by a hemorrhage soon undergo Wallerian degeneration in their distal fragments. That is in those parts separated by the lesion from their cell of origin, fatty changes become apparent by appropriate staining methods in from three to four days. Both axis cylinder and myelin sheath degenerate, and the

products of this disintegration are gradually absorbed so that at the end of three or four months removal is complete, and their place is occupied by a neuroglial meshwork or cicatrix. Degeneration also affects the proximal end back to the next adjacent or second node of Ranvier, rarely for a considerably greater distance. The cell of origin which has lost part of its fiber and become separated from its normal zone of distribution, also shows some alterations which are demonstrable by the proper histological methods. These changes are chiefly those of chromatolysis or solution of the Nissl bodies, giving the cytoplasm a pale homogeneous or very faintly granular appearance. Occasionally also the next neuronic link backward will show similar regressive chromolytic changes. This is the so-called retrograde or secondary degeneration or "réaction à distance" of Marinescô. A lesion of the internal capsule will result in Wallerian degeneration, absorption, and an ultimate glia scar of the pyramidal tract fibers actually severed, and chromolytic changes of the corresponding giant cells of Betz in the precentral gyrus. Destruction of the anterior horn cells or amputation of a limb may also show retrograde chromolysis of the Betz cells.

The immediate disturbance of function following a destructive hemorrhage is much greater than the ultimate or residual disability. This greater immediate effect is explained on the basis of the pressure exerted by the hemorrhage either directly, or through its effect on the circulation of the part, and by the concept of diaschisis of von Monakow. Pressure, *per se*, probably has little effect on the functional activity of the nerve cells. This is evidenced in the wide variations of intracerebral pressure experimentally recorded, and by the lack of disturbance, in a degree disproportionate to the actual structural losses found in hydrocephalus, brain tumor, etc. Hill has shown that no demonstrable disturbance takes place in the experimental animal with gradually increased intracranial pressure until this pressure rises to almost that of the arterial system, and concludes that the disturbances are those due to anemia through obstruction by compression of vascular fields. As a substantiating fact, he finds that lower pressures suddenly applied are more effective than gradual higher pressures, as in the latter case, the pressure in capillary and venous fields rises parallel to that applied.

By diaschisis is meant the disturbance in one structurally intact field, due to the sudden withdrawal from it of impulses, either of excitatory or inhibitory type which normally enter into its activity. Normal neuronic activity in a given unit is conceived as a state of equilibrium or balance, maintained by multiple stimuli convergently impinging upon it and the withdrawal of any one of these elements may result in disturbance of its normal function.

By far the most frequent site of cerebral hemorrhage is in the vicinity of the basal ganglia and optic thalamus, involving to greater or lesser degree the internal capsule and resulting in a hemiplegia. Next in order of frequence according to von Monakow come the centrum ovale, the cortex, the crura cerebri, the pons, and lastly the cerebellum. The greater vulnerability of the region of the basal ganglia led Charcot to investigate the blood supply of this region. For the most part the arteries involved are comparatively small ones given off by the great vessels at the base of the brain, and are true end-arteries in Cohnheim's sense, *i.e.* without anastomoses, a point which is of importance in considering the final results of hemorrhage, endarteritis, and embolism in this region. Duret, a pupil of Charcot, working under his direction at the Salpêtrière published in 1872–74, descriptions of the arterial supply of the region which have found wide acceptance. Huebner in 1872 published an account of the arterial system here which varied in some important points from Duret's, but which seems to have received little notice. In brief, Duret's findings were: (1) That branches from the anterior cerebral artery play an inconspicuous part in the supply to the basal ganglia. (2) That their chief supply comes from the middle cerebral which feeds the greater part of the caudate nucleus, all of the lenticular nucleus, a portion of the optic thalamus, and the whole extent of the internal capsule. (3) That the posterior cerebral plays a greater part than the anterior and supplies the greater part of the optic thalamus. These findings led to Charcot's insistence on the importance of the middle cerebral as the source of practically the whole supply to the basal ganglia and internal capsule, and to a part of the optic thalamus.

Duret divided the basal branches of the middle cerebral into three groups which he designated according to their distribution as (1) lenticular arteries, *i.e.* those whose distribution is to the globus pallidus; (2) lenticulo-striate which are distributed to the putamen as well, and (3) lenticulo-optic, whose distribution includes a part of the optic thalamus. He laid stress on the second group in relation to cerebral hemorrhage, and speaks of one of the larger branches particularly. He describes its course as skirting the base of the putamen near the surface in order to reach the nucleus caudatus, where it divides into four or five terminal branches, and says that it is this artery which should be designated according to his anatomical studies and the teachings of Charcot as the "artery of cerebral hemorrhage."

Huebner's description differs from that of Duret, in that he includes as of constant occurrence, a branch from the anterior cerebral artery to the head of the corpus striatum, and in that he found no instance, in thirty brains examined, of a lenticulo-optic vessel. The anterior part of the optic thalamus and the posterior limb of the internal capsule he found to receive their supply from a branch of the anterior choroid artery and from a branch of the posterior communicating artery. Beevor in 1907 by an ingenious method injected simultaneously and under the same pressure gelatine of three colors into the three main cerebral arteries. His diagrams of the sectional examination of such material show a large field of the head of the corpus striatum to receive its supply from the anterior cerebral. In 1909 there appeared in the *Boston Medical and Surgical Journal*, a report by H. F. Aitken made to Dr. J. B. Ayer of Boston, on the circulation to the lobar ganglia. Ayer concludes on the basis of this work that Charcot's assignment of the major share of supply of this region to the middle cerebral is incorrect. That the anterior cerebral artery gives off a constant contribution, and that the middle cerebral does not regularly supply any part of the optic thalamus. No case of lenticulo-optic artery was found in forty-five examinations. Numerous variations of the supply are of course encountered, but an important vessel or system of vessels arising from the anterior cerebral seems to be of constant occurrence, and occasionally the anterior cerebral proves to be the source of the principle striate artery. The accompanying figure taken from Aitkens report shows the general scheme of circulation of this area as found in his series of forty-five brains.

Leonard Hill's careful experimental work on the cerebral circulation has offered much of importance and interest in connection with cerebral hemorrhage.

Hill's method was that of injecting material under known pressure into the cranial cavity through threaded trephine holes in the skull, into which brass tubes had been screwed. At the same time similar tubes were connected to manometers to record changes in the pressure of the cerebrospinal fluid through the occipito-atlantal ligament and the cerebral venous

pressure through the torcular Herophili, while by means of cannula inserted into the general venous and arterial channels, changes in the pressure of the general circulation were observed. Pressure was then exerted on the brain by the injection of fluids or wax, or by the insertion of a rubber bag through a trephine opening, and its subsequent dilatation by means of

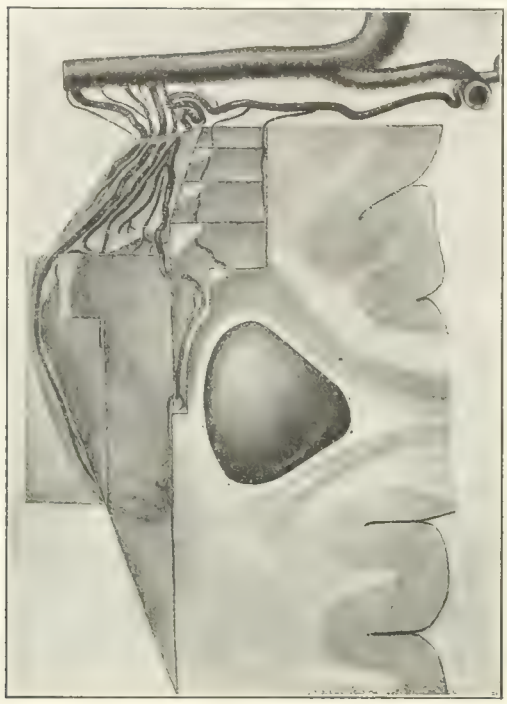


Fig. 1301. Showing the Origin of a Large Artery from the Anterior Cerebral. In this instance the vessel is unusually large and forms a principal striate artery. (Illustration by Aitken obtained through the kindness of Dr. J. B. Ayer Jr., of Boston.)

water at observed pressures. In other experiments, blood from one of the arteries in the trunk was led by means of a cannula and tube to the opening in the skull and there injected at its own pressure into the cranial cavity, thus closely approximating, experimentally, the conditions of pressure which obtain in spontaneous cerebral hemorrhage.

The brain is known to be practically inelastic and enclosed as it is in the rigid bony cavity of the cranium, the conclusion that pressure exerted locally at one point would be transmitted equally to all other parts of the cranial and spinal cavities, as would be the case with a fluid medium, seemed justifiable. Hill's experimental observations showed, however, that this was not the case. This absence of equal transmission is explained on the following basis: (1) The viscosity of the brain mass tends to prevent even translocation, and hence even pressure distribution. (2) The falx cerebri and tentorium cerebelli afford definite resistance to pressure. This is marked in both membranes, but is more prominent in the case of the tentorium, which forms an almost complete, and very resistant partition between the greater and lesser cranial cavities, thus protecting the cerebellum and brain stem to a considerable extent from pressure exerted over the hemispheres. The resistance offered by the falx cerebri leaves evidence which can frequently be seen on the autopsy table, especially in cases of subdural hemorrhage, as a distinct line or depression where the involved hemisphere had been pushed against the margin of the membrane. (3) Suddenly applied increase of tension results in the translocation of the brain mass downward, thus blocking the foramen magnum and preventing the rapid and ready transmission of pressure by cerebrospinal fluid into the spinal canal.

Hill points out that any increase of volume within the cranial cavity must result in reduction of the volume of either cerebrospinal fluid, or the blood contained in the extensive arterial, capillary, and venous systems. The part played by the cerebrospinal fluid in these conditions is not a prominent one. In the first place, the cerebrospinal fluid is probably present under normal conditions in small amounts only, and secondly, loss of fluid through its return into the veins will occur rapidly whenever conditions exist which tend to increase its pressure above that of venous pressure. The brunt then of the displacement in the cranial cavity, by the injection of a foreign body, including here for consideration the blood extravasation of a hemorrhage, is borne by the vascular system and results in the expression of blood from greater or lesser vascular fields dependent on the position and size of the injected mass. The fact that the viscosity of the brain mass is sufficient to prevent equal distribution of the pressure, results in greater expression of blood from those areas immediately adjacent to the foreign body. The conception thus indicated, *i.e.* that the symptoms of sudden increase in intracranial pressure are due to anemia from expression of blood from capillary fields—is beautifully supported by Hill's experimental work. The major symptoms of increase of intracranial volume are strictly comparable to those produced by sudden cerebral anemia, and appear experimentally when the intracranial pressure reaches that of arterial pressure. Below that point, the increase is compensated by a rise of capillary and venous pressure which results in the maintenance of flow until such time as the pressure reaches the arterial tension. In other words, the obstruction to the flow through a given vascular field by compression of its capillaries, results in transmission of greater and greater pressure until the resistance is overcome, except when this equals or exceeds arterial pressure.

The effects of discontinuity of pressure are, however, evident experimentally, as shown by the amount of displacement required to cause death in (1) the cerebrum, (2) the cerebellum, and (3) the medulla. Horsley and Spencer found that a foreign body of 6 to 8 c.c. in volume would produce death when applied over the cerebrum of the dog, while 2 to 4 c.c. was sufficient over the cerebellum, and 0.6 to 1.5 c.c. over the medulla.

In addition to the influence of the position of the hemorrhage on the occurrence of the major symptoms, the rate of outflow must be considered. In the production of anemia of the brain it can be shown experimentally that the rapidity with which the anemic state is reached, plays an important part in the type and the severity of the manifestations. Similarly rapid and slow injections into the cranial cavity give rise to different results, and the amount necessary to produce major symptoms is much greater when its introduction is slow than when it occurs suddenly. Large amounts of blood may be slowly extravasated into the cranial cavity. Bergmann records the finding of a blood clot weighing 180 grams. Similarly slow growing tumors may reach a relatively enormous size with comparatively small amounts of compensatory atrophy of brain substance by reduction in the blood volume of the cerebral vascular fields.

Hill's work with injections of serum and normal saline show the rapidity and ease with which fluids are absorbed from the meningeal spaces, and supports his view which is now widely accepted, that edema of the

pia cannot be a cause of increased intracranial pressure. Except in the case of rapid inflammatory transudate, such fluid cannot remain in the cranial cavity at a greater pressure than that of the intracranial venous circulation. From this viewpoint then, subpial edema as found at autopsy, must be the result of (1) cerebral atrophy, (2) inflammatory transudation, or (3) disturbance of circulation whereby some part of the normal intracranial blood volume is lacking. Hill states that "Serous apoplexy is an impossibility, and the operation of trephining in such cases as general paralysis of the insane, can receive no justification on experimental grounds."

Symptomatology.—The symptoms of cerebral hemorrhage may perhaps best be considered under several headings: (1) Prodromes; (2) symptoms of the stroke or attack; (3) symptoms of the period of reaction, and (4) chronic or residual symptoms.

True *prodromes* in the sense of those ushering in the infectious diseases, do not precede cerebral hemorrhage. There may be, however, various vague phenomena preceding the attack by a considerable period, though their occurrence is rare and care should be taken to exclude from consideration in this connection, cases of localizing brain disease of other types. Thus prodromes preceding a stroke due to syphilitic disease of the arteries or hemorrhages into a tumor mass, might give misleading data. Cases of hemorrhage established by autopsy examination do not, as a rule, show prodromes. Rarely, however, one does meet in this type, prodromes which antedate a hemiplegia. von Monakow considers these under two heads—general and focal. The general symptoms include irascibility, ringing in the ears, flashes before the eyes, hypochondria, forgetfulness, vertigo, headache, tendency toward somnolence, lassitude, speech disorders, etc. These are, as he points out, not characteristic and are common to a variety of chronic diseases, and as such are of little value. Of their possible relation to vascular disease which may later result in hemorrhage, nothing is known. The rare occurrence of focal symptoms is of greater significance. Facial pareses, dysarthria, diplopia, alexia and dyslexia, and unilateral subjective disturbances of the senses of heat and cold, numbness or tingling, or a feeling of weight in one-half the body are included among this group. Many of these are also associated with arteriosclerotic brain disease of a different type than that which leads to hemorrhage.

Déjerine, while recognizing the occasional occurrence of prodromes before cerebral hemorrhage, suggests that such symptoms are frequently of service in determining other causes for hemiplegic disturbances. Thus prodromal headaches, dizziness, and visual disorders suggest brain tumors; prodromal mental disturbances, general paralysis; tremors of the intention type, multiple sclerosis which occasionally is associated with a hemiplegia. Hemianesthesia without reflex disorders always suggests hysteria. Prehemiplegic pains on the side later affected by the paralysis are recorded by Weir Mitchell, Weisenburg, and others. They may exist for comparatively long periods—several years—before the actual attack. Motor disturbances of a paretic type may also be evident for a considerable time and ultimately be followed by a typical apoplectic stroke. No conclusive explanation of these phenomena is forthcoming. They are generally explained on the basis of poorly understood disturbances of nutrition in the area of distribution of the vessels, which are the seat of lesions, which in time result by rupture in a hemorrhage. In some of the more immediately preceding prodromes, slight blood extravasations at the site of miliary aneurysms or other lesions are offered as the causative factors. von Monakow records a case of rapidly fatal cerebral hemorrhage with prodromes lasting over the month preceding, in which a careful study of the brain revealed no definite explanatory lesions.

In the great majority of cerebral hemorrhages, however, the only prodromes are those associated with the immediate onset of the stroke, and even these may be lacking so that unconsciousness may come without warning.

The Attack.—Generally the attack comes on while the patient is in good health and often while at his ordinary occupation. Sometimes it is preceded by an unusua muscular effort, such as lifting a heavy weight, etc., or again it may occur during a period of rest or during sleep. Not infrequently the onset is on arising in the morning. In the typical case, there is a feeling of malaise, often a feeling of pain in one-half of the body and a word or two of complaint of the head, and unconsciousness supervenes. There may be a few convulsive or choreiform movements, or even a true convulsion early in the attack. In other cases the onset is more gradual and several minutes may pass between the first definite symptoms and final loss of consciousness, or the patient may still be conscious when paralysis first becomes evident. Again unconsciousness may not occur at all, but paralysis gradually appears. In still another form, the whole course of the appearance of symptoms is a slowly progressive one—gradual loss of power, mental confusion slowly developing into unconsciousness, and finally into deep coma—this is the so-called ingravescent apoplexy.

These variations in intensity of onset are dependent on three factors: (1) the site; (2) the amount of hemorrhage, and (3) the rate of extravasation. Comparatively large slow hemorrhages beneath the dura may give only slight symptoms, and similarly some cortical hemorrhages are associated with symptoms of rather minor severity. Oppenhein makes the statement that a rapid hemorrhage in the region of the basal ganglia, which reaches the size of a cherry or a hazel nut, is followed by a greater or less degree of unconsciousness. Hill's work on the dog gives an insight into the relation of rate of extravasation to the development of unconsciousness. Foreign bodies suddenly injected into the cranial cavity were effective in less bulk than those which were more slowly introduced. The slow injection gives time for the escape of cerebrospinal fluid from its spaces and of venous blood from the sinuses and larger vessels, thus making room for the foreign body without unduly compressing capillary fields.

Occasionally death supervenes rapidly after the stroke. This occurrence, as a rule, points to hemorrhage of the cerebellum, pons, medulla, or fourth ventricle, *i.e.* those structures beneath the tentorium where the pressure is confined and affects the important medullary centers. Abercrombie's case, with death within five minutes after the stroke is the shortest recorded, and proved to be a cerebellar hemorrhage which broke through into the fourth ventricle and thus produced direct pressure on the medulla. Death after one to two hours is more common in cases of hemorrhage near the medulla, while in severe hemiplegic apoplexy twelve to thirty-six hours more commonly elapse before a fatal issue. Occasionally after a short period of improvement including return of consciousness, a relapse occurs which is not infrequently fatal. This frequently follows the rupture of a hemorrhage into the lateral ventricles and occasionally in large subdural hemorrhages.

During the comatose period, the pulse is usually full, of high tension, and slow—about 50 to 60 per minute. With long-continued coma or in event of rise of temperature, the pulse rate may increase somewhat. In the fatal cases it becomes small, irregular and soft shortly before death and may disappear before respiration ceases.

Breathing is slow, deep, and stertorous and maintains about its normal ratio with the pulse. The face

is sometimes pale, but more frequently cyanotic, while the lips and cheeks are flaccid and are blown in and out loosely with each respiration. Not infrequently a clue can be gained to the existence of paralysis by observation of the relative range of motion of the two cheeks at this time. The flaccid, paralyzed side moving in and out a little more easily and loosely than the unparalyzed, which even in the deepest coma maintains some of its normal muscular tonus. Similar differences in the muscular activity of the two sides of the chest in respiratory movements may be noted. Cheyne-Stokes respiration may occur and is taken to be a distinctly unfavorable sign, referable to serious involvement of the medulla.

The temperature sinks after the stroke to 35.5° C. (95.9° F.) or below and rises again to normal or slightly above when resorption begins in the clot. This is usually within twelve to twenty-four hours, following the onset, and at this period a temperature of 38.2° C. (100.7° F.) need cause no undue alarm. Greater or more rapid rise, or rise at an earlier period is, however, considered as a distinctly unfavorable sign. Gowers observed a rise to 40° C. (104° F.) and 41° C. (105.8° F.) within an hour, in a hemorrhage into the pons and medulla. Hypostatic or insufflation pneumonia may also cause a rise of temperature and while these complications are serious they are of not quite so grave import as the rapid increase in temperature in their absence. The temperature of the two halves of the body may vary 0.5 to 1.0° C., that on the paralyzed side being lower than that of the normal. The period of inflammatory reaction may continue for from one week to two months, according to Osler, and the patient may die in this period, or if consciousness be regained there may be delirium or recurrence of the coma.

Generally the pupils are dilated, sometimes unequally. In deep coma they fail to react to light. In hemorrhage into the medulla or pons they may be strongly contracted even to pin-point size. When unequal, the wide pupil is usually on the side of the lesion. According to Hutchinson unilateral dilatation is associated with failure of the light reaction in that pupil.

Conjugate deviation, *i.e.* turning of the head and eyes toward the same side is not an unusual symptom. Its relation to the lesion is, however, a rather complex one. When the hemorrhage is in the cortex, and as usually its action is purely that of destruction, the head and eyes turn toward the side of the lesion, *i.e.* the paralysis of the muscles of the opposite side results in rotation by the greater pull of the tonic non-paralyzed muscles. When, however, the more rare effect of irritation by the hemorrhage is evident, the muscles which will later become paralyzed are in a state of spasm or convulsive contraction which results in turning the head and eyes away from the lesion. In the pons, however, where hemorrhage affects the fibers after their decussation, these conditions are exactly reversed, *i. e.* without spasm the deviation is from the lesion, with spasm toward it.

The occasional occurrence of convulsions at the time of the stroke may be explained by either of two conditions—anemia or irritation. Kussmaul and Tenner have shown that suddenly produced complete anemia of the brain results in convulsions, and Leonard Hill has demonstrated that the effect of a sudden increase in intracranial volume, at a pressure equal to that of arterial pressure, probably produces its effects by the production of anemia, by expression of blood from the capillary fields. True discharging or irritating effects of hemorrhage are rare, but when the lesion is in the cortex, or very close to it, such effects are occasionally observed, and may be the cause of the convulsions. Thus cortical hemorrhages occasionally give rise to one-sided Jacksonian convulsions which may recur over a period of several days. The parasthesias of the prodromal period must be considered as irritative phenomena of subjective type, but as a whole discharging effects of a hemorrhage are rare and of minor importance when contrasted with the destructive.

During the period of deep coma, the reflexes, both superficial and deep, are abolished. In lighter stupor, however, or when recovery from the coma has begun, the reflexes by their unilateral return give evidence of value concerning the side of paralysis. The time of return is variable—usually the reflexes of the non-hemiplegic side return with regained consciousness or slightly before, while on the affected side they are much delayed, sometimes for several weeks. The skin reflexes give evidence of value only when they are consistently unilateral. The abdominal cremasteric and scrotal reflexes may be absent or very slight in the normal individual. This is especially true of the abdominal in cases with excess of fat or relaxed abdominal walls. Erection of the nipple and wrinkling of the areola on stimulation of the skin of the breast near the areola, in both males and females, *i.e.* the nipple reflex, may by its unilateral absence, add to the available data.

Babinski's reflex, dorsal flexion of the great toe on stimulation of the sole of the foot, or the allied Oppenheim and Gordon reflexes may be an early and important sign of the side affected, as may the unilateral absence of the patellar and achilles reflexes. Later the deep reflexes of the affected side become increased.

The muscles may during the period of coma indicate the affected side. While both sides at this stage are relaxed, the flaccidity of the hemiplegic side may be greater than the opposite as is evidenced by the looser movements of the cheek with respiration mentioned above, the more rapid and flail-like fall of passively raised extremities and less resistance to passive motion. Observation of the large muscle masses such as the thigh may show that those of the paralyzed side hang loosely from the bones like semi-fluid masses in contrast to the unaffected.

The frequent association of aphasia and its concomitants with right-sided hemiplegia in right-handed individuals and *vice versa* in left-handed ones, makes the determination of the paralyzed side of importance from a prognostic standpoint.

Urine and feces are usually passed during the comatose period—rarely there is retention. This is, however, not a permanent condition, as the sphincters are not affected by the residual paralysis. The amount of urine passed during the first day or so after a stroke is abundant—probably due to the increased blood pressure. Albumin may be present in small amounts in occasional cases, but is then probably referable to nephritis, rather than to the apoplexy. Sugar is not infrequently found early in the attack in small amounts. When in large quantity or present over a long period it probably refers to severe involvement of the medulla either by direct damage or indirectly through pressure, and is of the gravest significance.

Trophic changes of the skin may appear within forty-eight hours of the stroke and are then of unfavorable import. Sloughing eschars of the thigh or sloughing and vesiculation of the skin are included here, while some also consider the congestion and edema of the dependent portions of the lung as trophic in origin. The explanation of these latter phenomena, as results of disorder of circulation from interference with the bulbar nervous mechanisms, seems more acceptable.

If death does not occur in the first few hours after the stroke there are evident, usually, gradual signs of improvement. The deep coma slowly gives way to stupor and this to a heavy somnolence in which returning consciousness is evident from the occasional opening of the eyes and sluggish, purposeless, or tossing motions of the non-paralyzed limbs. The mind is, however, often markedly confused and the outward reaction to disturbance is surly, sullen, or morose. There is with the confusion a noticeable apathy like

that of oppressive somnolence. Yawning may be prominent. Speech if attempted is almost always slow and difficult and answers are often irrelevant or confused. Articulation, while slow and evidently only carried out with effort, is comparatively undisturbed, though in cases of right hemiplegia in right-handed persons there may be distinct evidence of motor aphasia. Occasionally the confusion may be replaced by slight delirium. The pulse gradually increases in rate and is usually of lower tension. The respiration becomes less labored and the temperature rise described above may be made out. The skin becomes warmer and moist. With returning consciousness, complaint may be made of pains or parasthesias—formication is not infrequent—in the paralyzed limbs.

Reaction.—These conditions lead up gradually after twenty-four to forty-eight hours to the reaction stage in which the patient, while conscious, oriented, and with clear mental grasp on surroundings, shows sleepiness, apathy of varying degree, and exhibits anorexia, disturbances of digestion, frequently inordinate thirst, and complains of headache or a sense of pressure in the head. This group of symptoms is generally referred to the stage of early reaction around the blood clot and parallel such change closely in time. They are variable in their intensity and in duration. Von Monakow states that their duration is from two to six weeks in case of a hemorrhage the size of a hazelnut or walnut in the neighborhood of the basal ganglia.

During this period observation can be made with sufficient accuracy to give considerable evidence concerning the site and relative destructiveness of the lesion.

Paralysis is in the usual type of case, the most prominent symptom and commonly this is of the hemiplegic type—*i.e.* leg, arm, and face of one side. No attempt will be made here to give a full review of regional diagnosis, but some combinations are so well illustrated in cases of hemorrhage that they may well be included briefly.

With a cortical lesion, unless very large, the paralysis is of monoplegic distribution, or limited to a part of one limb. In internal capsule hemorrhages (the most common type), the distribution is that mentioned above, *i.e.* arm, leg, and face of one side. The eye muscles are not, however, involved and there is a considerable variation in the severity of involvement of the various regions of the affected side. The arm usually suffers more completely than the leg. The involvement of the face may be severe together with an arm, but in this case the leg is less affected. Less commonly the leg bears the brunt of the attack, and in this case the facial disturbance is usually comparatively slight. Facial paralysis is readily made out, but here again the involvement is apt to be incomplete—the upper segments suffering relatively less, so that the frontalis muscle and the orbicularis maintain their activity. Even in complete facial paralysis of this central type, bilateral movements, such as those of laughing, crying, etc., are preserved. The paralysis is, however, readily apparent on any attempt at volitional motion such as whistling. The tongue is also involved, and when in the mouth, its tip is turned toward the sound side of the body (*i.e.* toward the brain lesion), due to the greater bulk of the relaxed intrinsic muscles. When protruded, its tip points toward the paralyzed side (away from the brain lesion) from the unopposed action of the non-paralyzed muscles. Lesion of the crura cerebri gives a group of symptoms known as Weber's syndrome—hemiplegia of the type described above, but complicated with a peripheral or lower motor neurone paralysis of the oculomotor group of the opposite side of the body (*i.e.* same side as the lesion). Hemorrhage into the pons and medulla give a similar type of crossed paralysis except that in this instance, the eye muscles will be free and the face or tongue or both, of the side opposite to the arm and leg will be paralyzed.

Examination of the skin sensations generally shows a decrease or loss, occasionally an increase, of the sensations of pain, touch, and temperature. During the stage of reaction there is always, according to von Monakow, a difference in the sensation of the two sides and its distribution is similar to that of the paralyses, *i.e.* a leg suffers more severely than an arm or *vice versa*. Total hemianesthesia is usually of functional origin and is very rare in hemorrhage. As with motion the distribution depends on the side of the lesion. Strictly monoplegic loss of sensation is usually the result of a cortical lesion and crossed anesthesias are of bulbar or pontine origin. According to Osler, bulbar lesions affecting the fifth cranial nerve are apt to exhibit a syringomyelic type of dissociation of touch from pain and temperature sense. Generally the sensory disturbances disappear rapidly and very much more completely than the motor. When this is not the case it points to a lesion involving the posterior limb of the internal capsule. Correlation between severe involvement of the leg (posterior part of the anterior limb of the internal capsule) and the degree of anesthesia (adjacent posterior limb fibers) is occasionally possible. The reflexes at this stage begin to take on the characteristics of the chronic or residual stage. The deep or tendon reflexes on the paralyzed side are increased. Babinski's sign and ankle clonus are present. In the majority of cases, the skin reflexes return and are apparently equal on the two sides. Sometimes, however, especially in those cases where the sensory loss is disproportionately great, they may remain reduced or may even be absent.

Occasionally there occurs in the comatose period or early in the period of reaction, a rigidity or spastic condition of the muscles of the involved side which is probably of the nature of a discharge through irritation. This is called early or primary rigidity and generally disappears early.

In the special sensations many types of disturbances may be apparent. The commonest is incomplete homonymous hemianopsia. Gowers states that hemianopsia may be expected in cases in which conjugate deviation of the head and eyes has been prominent during the comatose period.

Symptoms of grave cerebral disorders, such as aphasia, alexia, agraphia and apraxia may be manifest at this stage, but it is well to bear in mind that speech is almost always slow and labored at this time, and that slight confusion may interfere with proper and relevant replies, and apathy may to some extent mask the reaction. This dysarthric disturbance, however, tends to disappear rapidly except when the speech centers or paths are involved as is quite frequent in right-sided hemiplegia.

Subjective disorders may be evident in the form of mild hallucinations of the special senses. As a rule these are, however, associated with insight into their pathological origin, and do not carry with them the convincing sense of objective reality of the hallucinations of some mental disorders. In general, hallucinations may be regarded as rare unless one includes in this category as hallucinations of the common sensory sphere, those subjective feelings of numbness, tingling, formication, etc. which so frequently usher in a stroke and which are probably of the same origin. When the hallucinations are presented in the special sensory spheres, they form an important clue to the site of the hemorrhage, which is sometimes of prognostic value. Thus hallucinations of sight are apt to be followed by permanent hemianopsia, etc.

Residual Symptoms.—The chronic symptoms or, as more commonly known, the residuals, like the symp-

toms of the third period vary markedly in distribution and severity, depending on the site and amount of destruction at the point of lesion. The greater number of hemorrhages result in hemiplegia through involvement of the internal capsule, but the amount of destruction here and consequently the permanent disability vary greatly. The brunt of the destruction of most hemorrhages of this neighborhood is borne by the basal ganglia, and as a rule only a part of the capsular fibers undergo complete severance. Immediately after the stroke, however, a considerable part of the surrounding substance is involved either by pressure and consequent anemia or by reactive edema, which interferes with the functional activity of parts which are not destroyed. During resolution and resorption of the clot, however, these conditions are markedly alleviated and the paralysis undergoes a parallel improvement so that it is usual for a considerable amount of muscular control to be recovered in at least some part of the paralyzed side. The recovery follows the order outlined above. The arm is usually the last to show improvement and remains with the greatest permanent disability. More rarely the leg bears the brunt. Occasionally the whole of the pyramidal tract is broken through in the capsule and permanent total hemiplegia results. The paralysis of of the face generally undergoes marked improvement. In some cases practically all of the paralysis disappears, but such recovery is unusual in hemorrhage and should make one suspect cerebral syphilis, or the apoplectiform attack of early general paralysis. In hemorrhage, the recovery is rarely complete and while the leg and face may regain their activity and some power may be restored to the arm, the finer motions of the hand will be lost permanently. The recovery is gradual and variable and no definite period can be assigned. Osler says that when hemiplegia has persisted for three months and contractures have developed, the condition is past relief. The classical residuals are a more or less complete paralysis of the arm with contracture which draws the arm into a characteristic position, but recovery in the leg sufficient to allow the patient to get about with a limp. The hemiplegic gait is characterized by a stiffness of the affected limb with a tendency to dragging of the toes and a pivotal motion of the hip, whereby the paralyzed leg is lifted from the ground by tilting the pelvis up on the sound leg as a fulcrum and then a swinging forward, often in more or less of a circular sweep of the pelvis and paralyzed leg about the sound hip as a pivot.

The muscles become spastic and the deep reflexes exaggerated on the affected side. This is a constant result of lesions of the pyramidal tract, and is probably due to the withdrawal of the inhibitory activity of the corticospinal neurone with preserved activity of the gangliospinal, deiterospinal, rubrospinal, and other neurones tending to maintain tonus in the spinomuscular system, or final common path. The corticospinal, or volitional motor path seems to hold a certain degree of prepotence over the lower motor neurone, or final common motor path, for the maintenance of which it is essential that the continuous flow of impulses from the kinesthetic apparatus and adjuvant motor paths be held in partial check, in order to prevent an overriding by them of the volitional impulses, and it is the withdrawal of this check or inhibition which results in the spasticity and increase of reflexes.

Marked atrophy of the paralyzed muscles is rare. It is not uncommon to find some reduction as contrasted with the sound side, but much of this is probably the result of trophic disturbance of a less direct type than that of lower motor neurone disease, and is not associated with any alteration in the electrical reactions of the muscles, or the peripheral nerves. Occasionally, however, marked atrophy may result, which has generally been considered to be due to secondary involvement of the lower motor neurone. Cases are recorded, however, in which postmortem examinations have revealed normal anterior horn cells in the corresponding segments. The mechanism of this type of muscular atrophy of cerebral origin is obscure. In hemorrhages resulting in paralysis in childhood, it is common to find that the affected limb has not kept up in growth and development with the normal. This is to be distinguished from that described here, *i.e.* atrophy setting in in the adult. .

Occasionally the affected limb maintains the condition of flaccidity of the early period. This is usually in paralysis occurring early in life. Generally the spasticity is marked and contractures develop. The arm usually shows the greatest amount of contracture (secondary or late rigidity). Permanent flexion of the elbow on the arm, of the wrist on the forearm, and of the fingers on the hand, with adduction and slight limitation of the movements of the shoulder, make up the features of the characteristic result. There may be considerable pain with the development of contractures. The leg rarely suffers so much, but in bedridden cases, it is not unusual to see the leg fixed in flexion, and adduction at the hip, flexion at the knee, and plantar flexion of the foot and toes. In some patients with sufficient recovery to be about, flexion at the knee and plantar flexion of the foot modify the typical gait, the partly bent limb swinging forward from the pelvis without the circumferential swing mentioned above.

There are frequently evidences of trophic disorder of more or less severe grade. The early and very rapid decubitus has been mentioned. Decubitus of the more ordinary and slowly developing type is not uncommon in bedridden cases and is usually troublesome. The skin of the parts showing the greatest residual effect is cool, dry, tense, and shining, and gives the impression of thinness. Slight edema of the paralyzed parts is frequent. Arthropathies are apt to develop and in cases where contracture has been marked the joints may be firmly fixed so that separation of all of the inserted muscles on the autopsy table will still not permit of straightening out of the limb, without the application of considerable force.

In hemiplegia in children, epilepsy, chorea, or athetosis may result. There is some question here, however, whether these results are not at least more commonly, if not constantly, associated with lesions resulting in marked gliosis, than with true hemorrhagic lesions. Occasionally, however, the jerky purposeless movements of chorea, or the rhythmic, sinuous orderly movements known as athetosis, may occur in the paralyzed limbs of cases of cerebral hemorrhage in the adult.

Recent work on the region of the basal ganglia suggests that the choreiform movements may be the result of damage to the lenticular nucleus and the athetosis to discharging lesions of the optic thalamus. Epilepsy is an occasional result—this again is more common in children than in the adult. Another rare result of early hemorrhage is the phenomenon of associated movements in which the paralyzed limbs respond to efforts of volitional motion on the sound side.

Motor aphasia is an important and not infrequent concomitant of hemiplegia from hemorrhage in the left hemisphere (right hemiplegia) in right-handed individuals and *vice versa*.

Various mental disturbances may follow in the train of cerebral hemorrhage, varying in type from minor emotional instability to severe grades of dementia. The latter do not, however, seem to accompany so frequently the classical type of hemorrhage as the attacks of cerebral softening associated with advanced, widespread cerebral arteriosclerosis.

Diagnosis.—During the comatose period, diagnosis is frequently difficult. When consciousness has been

regained and paralysis or hemianopsia is present, hemorrhage is easily differentiated from most of the conditions with which the comatose period might be confused, but it is often very difficult to distinguish between a hemiplegic or other destructive attack due to hemorrhage and that due to cerebral softening. From all other conditions, however, unilateral alterations of the reflexes or rigidity, or undue flaccidity of the muscles of one side of the body are important and practically diagnostic.

In simple syncope, the pulse is usually small and in sharp contrast to that in a case of apoplexy. There is also little or no stertor and the face is pale rather than cyanotic, and the unconsciousness is not so deep, and rather short lived.

In uremia if a sample of the urine can be obtained by catheterization it will often give a clue to the origin. It must be remembered, however, that cerebral hemorrhage is not infrequently a complication in Bright's disease and hence too much dependence must not be placed on a urine examination. This is especially true of the albuminuria which frequently occurs in cerebral hemorrhages. Microscopic examination of the sediment may give clearer facts. The presence of edema, especially of the feet and beneath the eyes, the occurrence of albuminuric retinitis, and the peculiar pasty anemia of chronic nephritis are all very valuable evidence pointing toward uremia. Tyson says that coma in a puerperal woman associated with dropsy and albuminuria means Bright's disease. Usually uremia does not appear with the suddenness of hemorrhages, but gives warning over some time preceding the onset of unconsciousness.

Diabetic coma may be mistaken for apoplexy. Examination of the urine or the odor of acetone on the breath gives important clues. It is well to remember, however, that sugar may appear in the urine in considerable quantities in hemorrhages involving the medulla. Here again as in uremia, the onset is rarely as rapid as in typical cerebral hemorrhage.

Coma from acute poisoning by narcotics, especially alcohol, opium, and chloral and chronic poisoning by lead may give difficulty. The odor of alcohol on the breath in the absence of history of marked excesses cannot be depended on, as not infrequently an alcoholic debauch is the exciting factor in a hemorrhage. Opium or morphine poisoning gives rise to the pin-point pupil, but as has been mentioned above a similar result may occur from hemorrhage into the pons, medulla, cerebellum, or fourth ventricle. The cool, livid skin and rapid small pulse of opium poisoning with the difference in temperature of these two conditions are points of importance. In poisoning by chloral and other narcotics, it is often impossible unless a history of the administration be obtained, to reach a diagnosis during the comatose period. Here, however, it may be well to mention again unilateral reflex disturbances and inequality of the muscle tonus of the two sides. Chronic lead encephalitis occasionally results in attacks of coma. The anamnesis and other signs of chronic lead poisoning will usually make diagnosis easy here.

In hysterical coma, the eye reflexes and deep reflexes are not disturbed. This is of course also of value in diagnosis of an hysterical hemiplegia following the coma.

The coma following an epileptic convulsion offers difficulty, especially when it is borne in mind that convulsions may usher in large sudden hemorrhages such as those that rupture into the ventricle. Unilateral symptoms are lacking and a fresh wound or old scars on the tongue may aid. History of previous attacks may be obtainable.

Apoplectic attacks occasionally occur in the course of growth of a brain tumor. Probably these are dependent on hemorrhages into the tumor mass, though other causes may play a part in the sudden variations of intracranial pressure here. History of headache, projectile vomiting, and localizing signs of brain disease will aid, while an ophthalmoscopic examination usually reveals a choked disc.

Similar attacks are of some frequence in the course of general paresis or paralytic dementia. They tend, however, to clear up rapidly, leaving little or no clear-cut residual paralysis. Most of these cases will have shown the various mental manifestations of the early stages of paresis before the attack, though occasionally the stroke is the first thing to receive notice and the mental symptoms are dated by friends from that time. Rapid disappearance of paralysis with remaining bilateral reflex alterations such as increase or decrease of the knee-jerk, double Babinski, or double ankle clonus, the Argyll-Robertson pupil, and the characteristic slurring speech defect are usually of great aid, while the application of the more recent laboratory tests, such as the Wassermann reaction of the blood and of the spinal fluid, and further tests of the fluid for protein, cell content both in numbers and differentially, places the diagnosis among the most definite of any of the brain diseases.

Injury to the head should be excluded when a case with no history available is seen first in the comatose period.

Acute hemorrhagic encephalitis may commence with loss of consciousness, but usually this stage is preceded by marked premonitory symptoms, such as headache, confusion, or a delirium which is sometimes very active, and the temperature in this condition is high and the reflexes are not so completely abolished as in hemorrhage.

Unconsciousness from rupture of an aneurysm or rupture of the heart, or from an acute paralysis of the heart, may be differentiated usually with some security by the condition of the pulse.

Diagnosis between cerebral hemorrhage and encephalomalacia, due to thrombosis and embolism, is difficult and often impossible. The age of the patient may give a clue. Hemorrhage, as can be seen from the above table, is distinctly less frequent before the age of forty. Thrombosis and embolism are more so. The association of thrombotic or embolic processes elsewhere in the body will of course aid. As a rule, thrombosis is accompanied by much more gradual onset of symptoms than hemorrhage, though rapidly forming thrombi may give rise to symptoms closely paralleling ingravescent apoplexy. When the thrombus is septic an elevation of temperature is to be expected. Embolic foci of softening do not give as a rule the secondary rise of temperature which is explained in hemorrhage on the basis of inflammatory reaction about the clot. The clearing up of the paralysis except in those parts whose central connections have been actually severed is much more rapid in embolic softening than in hemorrhage. Softening from syphilitic endarteritis may also be difficult to distinguish. Generally, however, in this type prodromes in the form of pareses or paresthesias have been noted and the depth and duration of the coma are less than in hemorrhage. Here again the serological and cytological findings are important. Concomitant heart disease, especially acute valvular conditions, or history of chorea, or rheumatism with valvular lesions all suggest embolism.

Prognosis.—The prognosis as to both life and the extent of recovery following a cerebral hemorrhage is dependent on two prime factors—the site and size of the extravasation. The mortality table by Jones, in Lewandowsky's Handbuch der Neurologie, which is included in the article dealing with disturbances of the cerebral circulation is here repeated as of interest.

	First 24 hours.	To end of first week	To end of first month.
	Per cent.	Per cent	Per cent.
Cerebral hemorrhage	37.7	72.5	86.2
Ventricular hemorrhage	60.0	90.0	
Cerebral thrombosis	8.7	30.4	60.8
Cerebral embolism	0.0	30.7	30.7

Lewandowsky suggests that the figures here for cerebral hemorrhage are too high, as they were made from autopsied cases in a large hospital and consequently contained a large percentage of the severer types.

There are, as suggested under the heading of symptomatology, many symptoms which indicate a guarded or unfavorable prognosis. Rapid or early, or unusually high rise of temperature is an unfavorable sign. In general, it may be said that the longer the period of deep coma, the more grave is the prognosis. A rapid small pulse is unfavorable. Hemorrhages into the medulla are almost always fatal, into the pons frequently so, hence symptoms pointing to involvement of these structures are always of the gravest import. Of these, the commonest are Cheyne-Stokes respiration, crossed paralyses, and contraction of the pupils, while occasionally vomiting and sugar in the urine are noted. Early and advancing decubitus as pointed out by Charcot and others is almost always a fatal indication. Pneumonia and congestion and edema of the lungs are frequently the cause of death following hemorrhage, and must always be considered as very serious complications even though the involvement be of minor grade. In the ingravescent form the prognosis is bad. In cases of rapid recovery from an apoplectiform attack with little residual effect, one must consider general paralysis and cerebral syphilis and if these be determined, the prognosis must be altered acordingly.

With regard to improvement in those cases in which the outcome is not fatal early in the attack, it may be said that there is almost always a considerable regain of function in the paralyzed areas, but also that there is almost always some loss of muscular power or control. This is especially noticed in the finer movements in the hand. Hemianopsia is apt to improve, but if well marked on regaining consciousness there will probably be a residual permanent loss. Anesthesias and paresthesias are very much more apt to disappear than paralyses. The early dysarthria of returning consciousness generally completely disappears, but if aphasia is present, the prognosis should be more guarded, for while recovery sometimes takes place and improvement is the rule, there is occasionally a permanent defect. The prognosis of an aphasia associated with hemiplegia is, however, relatively much more favorable than other types of aphasia. It is well even early in the attack to give a guarded prognosis in right hemiplegia in a right-handed individual on account of possible permanent aphasia.

Occasionally an apparently complete recovery follows a cerebral hemorrhage. This seems more frequent in small cortical lesions, especially of the "silent areas" of the brain. These cases are rare enough, however, to be excluded from consideration in giving a prognosis. Nearly always there is some residual mental or physical defect of greater or lesser importance. Tyson states that a stroke of paralysis is justly regarded as a blow which marks the beginning of inevitable decline in health and usefulness. Slight alterations in emotional stability are very frequent, and occasionally a cerebral hemorrhage marks the beginning of dementia. Second and third attacks are not infrequent and the prognosis is progressively less favorable in each. Anything tending to increaes the diseases associated with high blood pressure, such as chronic nephritis, hypertrophy of the heart, or arteriosclerosis, naturally makes the outlook more serious. Finally as to prognosis of the recovery of functional activity in the paralyzed limbs, Osler states that if paralysis is present at the end of a month some grade of permanent palsy is certain to remain. The supervention of late rigidity is to be considered the end of the period of recovery.

Treatment.—Treatment will be considered under the following heads: (1) prophylactic; (2) treatment during the attack; (3) treatment of the residuals and general treatment after the attack.

Under the head of *prophylaxis* is included the various measures aimed at the underlying causes of chronic increase of arterial tension, such as nephritis, cardiac hypertrophy, and arteriosclerosis. Our knowledge of the etiology of miliary aneurysms is so meager that nothing in the way of specific prophylaxis can be indicated. When, however, undoubted prodromes of focal brain disturbance are present all excessive physical strain should be avoided. Alcohol should be prohibited or used very sparingly. Mental exhaustion and sudden emotional stress are also to be avoided.

During the attack, treatment is largely dependent on a correct diagnosis, as measures adopted in cerebral hemorrhage are contraindicated in softening from thrombosis and embolism. In either condition, the patient should be kept quietly and comfortably in bed with the head slightly raised and the neck free. Absolute quiet and freedom from emotional stress should be assured even by the exclusion of members of the family if necessary. In the event of marked dyspnea and signs of mechanical respiratory disturbance, a position on the side instead of on the back will sometimes aid in preventing congestion of the bases of the lungs. It is probably better to place the patient on the sound side, thus rendering more easy the return of blood from the lung of the paralyzed side where respiratory motions are somewhat limited. Care must be taken, however, that this position is not maintained if it tends to increase the respiratory difficulty. Enemata and mild laxatives are indicated in both conditions.

If the diagnosis of cerebral hemorrhage is certain, measures for the relief of the high blood pressure are usually advised. This is one of the conditions in which venesection still finds employment. Probably equally effective is free purgation. It appears, however, from experimental results that the rise in blood pressure is a compensatory effort on the part of the vasomotor mechanism to overcome the resistance to cerebral circulation caused by the rise of intracranial pressure. This is particularly true in the progressive rise of pressure accompanying a continuing hemorrhage and here, especially, if the hemorrhage be subdural, craniotomy and removal of the clot may be considered. Even in other types of hemorrhage, Hill advises decompression on experimental grounds. He offers the warning, however, that a small opening will probably prove ineffective and that either the clot must be reached and removed, or the opening must be of such size as to permit of compensatory expansion of the cranial contents equivalent to the amount of the clot, and that even here, the viscosity of the brain may prevent effective relief. Surgical removal of the clot would undoubtedly serve to hasten recovery of some of the primary paralysis, and relieve the secondary symptoms associated with the period of resorption and might reduce the amount of the residual or permanent disability.

Ice packs and other locally applied measures to

the head are without justification, but as Oppenheim suggests, are harmless and may be applied if desired.

Horsley and Spencer recommended, on experimental grounds, compression of the carotid artery in ingravescent cases.

Venesection and purges are contraindicated in cases with slow, feeble pulse and in embolism and thrombosis. Drugs are not of especial avail, though they may be exhibited to meet individual symptoms. Strychnine is occasionally of value as a stimulant. Digitalis should not be used. Mild hypnotics may be required to control restlessness, insomnia, or headaches. Diet should be light and readily assimilable, and indigestion should be avoided, especially if provocative of vomiting with its concomitant danger of insufflation pneumonia. Potassium iodide is frequently administered to promote absorption, but its use except in syphilitic cases is of doubtful value.

The paralyzed limbs should be kept warm and in a comfortable position, but care must be taken with hot-water bottles as the trophic disturbances render the skin more susceptible to burns, and consequent troublesome sloughs, than in the normal. Attention to cleanliness is necessary to prevent decubitus in those cases where the patient is in bed for some time.

Treatment of the Residuals.—Within a few days after the attack gentle massage and passive motions of the paralyzed limbs may be begun. The massage should be gentle and toward the body to promote return circulation. Passive motions should be carefully made and not excessive in sweep. Within two weeks or longer in very severe cases electrical applications may be made to the paralyzed muscles. Faradic application seems the most satisfactory. When contracture begins to be apparent it should be applied to the antagonists of the contracted muscles only. Active gymnastics of the recovering muscles may be tried, but should be started very gradually and employed cautiously. In advanced contracture with marked deformity and pain, tendon transplantation or section of the nerves or nerve anastomoses may be tried.

The development of contractures generally marks the end of the stage of improvement, and further exhibition of electricity massage, etc., is justifiable only for the amelioration of the effects of the contracture.

One attack of cerebral hemorrhage gives evidence of cerebral vascular disease which may lead to others, and hence a well-regulated life with the avoidance of exertion or mental or emotional stress is to be advised.

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Cerebrospinal Fluid.—*Synonyms:* celiolymph; liquor cerebrospinalis.

ANATOMY.—The cerebrospinal fluid is found in the encephalic and myelic ventricles, and in the subarachnoid and subdural spaces. It varies in amount from 60 to 200 c.c., increasing somewhat with age. It is not lymph and is sufficiently characteristic in its reactions to be distinguished from other serous fluids. The subarachnoid space is the interval between the arachnoid and the pia, very narrow on the upper and lateral aspects of the encephalon, crossed by numerous bands of arachnoid tissue, but enlarged in certain regions at the base, above the corpus callosum and over the optic lobes, called the cisternæ subarachnoidales.

These are in communication with one another and have as tributaries the clefts along the great fissures (flumina), which themselves have as tributaries the spaces along the secondary and tertiary fissures (rivi and rivuli of Duret). There are prolongations of this space around the optic, olfactory, and auditory nerves, and a connection with the lymph spaces around the other cranial and spinal nerves. Communications with the lymphatic vessels of the nasal mucous membrane and deep vessels and nodes of the neck also exist. These connections have been demonstrated by the injection of the subarachnoid space with colored fluids which have filled the lymph vessels of the nasal mucous membrane, traversed the lymph spaces of the nerves, and penetrated the deep cervical vessels and nodes. The colored fluid has also been observed to pass into the dural sinuses through the arachnoidal villi, probably indirectly by filtration. Flatau,[1] by the injection of colored fluids, was able to make them escape from the nose. Naunyn and Schreiber, quoted by Flatau, have demonstrated the same thing, using salt solution, the flow from the nose being accompanied by protrusion of the eyeball and chemosis.

According to Binswanger and Berger[2] the subarachnoid space also receives the lymph from the adventitial lymph spaces of the cerebral cortex. They observed that in cases of intraventricular hemorrhage in the human subject, blood would make its way into the subarachnoid space and thence into the intra-adventitial spaces of the cortex. Injection of a carmine mixture into the subarachnoid of a dog likewise filled the cortical intraadventitial spaces. These observations confirm those of Key and Retzius.

Subdural injection of colored material has demonstrated the following connections with the subdural space (Schwalbe[3]): (1) The deep lymph vessels and nodes of the neck. (2) The subdural spaces of the nerve root and lymph paths of peripheral nerves (Key and Retzius). (3) The lymph paths of the dura through fine clefts (Michel). (4) The dural sinuses through the arachnoidal villi.

The ventricles communicate with the subarachnoid space by the foramen of Magendie (metapore) and the aperturæ laterales (foramina of Luschka). The connection described by Merkel and Mierzejewsky in the descending horn of the lateral ventricle is probably an artifact. The existence of the metapore and the aperturæ laterales has recently been confirmed by Blake.[4]

There is no direct connection between the subarachnoid and subdural spaces, but the lymphatics of the nasal mucous membrane, the lymph spaces of the nerves, and the cranial sinuses through the arachnoidal villi can be injected from both cavities.

The histology of the choroid plexuses of the lateral ventricles has recently been investigated by Findlay,[5] who finds that there are for the most part several layers of cells on the villi and that the surface cells may contain globules which are extruded, leaving the empty cell membrane. These globules may be found in the ventricular fluid. They darken with osmic acid and are probably fatty in nature. Yoshimura[19] has shown that glycogen, fibrin, lecithin, and fat exist in the cells of the choroid plexus, and Pellizzi[20] that the fat is tripalmatin and tristearin.

Blood-vessels are very numerous in the choroid plexuses, and nerves too have been demonstrated in the plexuses of the lateral and fourth ventricles (Benedikt), so that structurally they are secretory in character.

The morphological elements are very scarce in the

normal fluid and consist of a few leucocytes, endothelial cells, and occasional globules of a fatty nature derived from the cells of the choroid plexuses.

The experiments of Key and Retzius,[6] confirmed by Kollman, seem to show that one of the outflow paths for the subarachnoid and subdural spaces is by the way of the arachnoidal villi into the cranial sinuses. Other paths are along the cranial and spinal nerves to the general lymphatic system. More recently it has been demonstrated that normal saline solution tinged with methylene blue and injected into the subarachnoid space can be traced passing into the sinuses and veins, and in a few minutes the blue is found in the stomach and bladder; but it is only after one hour of steady injection that the deep cervical nodes begin to be tinged. The rapid absorption then takes place rather by the blood-vessels than by the lymphatics.

The amount of cerebrospinal fluid increases with age and with brain atrophy, and decreases in those diseases in which the volume of the brain is augmented; it also varies with the amount of blood in the intracranial vessels.

Physiology.—The cerebrospinal fluid forms a water-bed on which rests the base of the middle and posterior parts of the encephalon. It performs an important function in protecting the brain from injury and the circle of Willis from compression. It also helps to dissipate the force of a blow, so that less injury is done at the point of its reception. This may result in a disruption of brain substance in a region far removed from the place of injury. For example, a blow received on the front of the head in a direction downward and backward may cause hemorrhages in the region of the medulla and fourth ventricle, as a result of the ventricular fluid trying to pass through the narrow aqueduct of Sylvius (Park[7]).

Sudden tapping of this water-bed may occasionally result in injury to the brain from the sudden changed relations of the encephalon to its rigid bony case; also when the ventricles have been distended, the sudden withdrawal of fluid may leave parts unsupported, resulting in injury to the brain tissue.

According to A. and E. Cavazzani[8] secretion and absorption of the cerebrospinal fluid proceed slowly. To test the rate of secretion, ferrocyanide of potassium was injected into the peritoneal cavity of a curarized dog. The salt did not appear in the cerebrospinal fluid until after an hour had elapsed.

To test the rapidity of absorption the posterior occipito-atlantal ligaments were opened and 4 c.c. of a fifty-per-cent. solution of iodide of potassium was injected into the arachnoid space, and the same solution wa also injected into the encephalic arachnoid cavity. The salt was found in the urine in a minimal time of twenty minutes, and a maximal time of two hours. The great difference of time in absorption was accounted for by the variations in pressure of the cerebrospinal fluid and the blood.

Thomson's[9] observations, in several cases, of the spontaneous flow of cerebrospinal fluid from the nose show that the secretion may be quite rapid, the flow averaging 500 c.c. in twenty-four hours. Hill[10] has shown that the rate of secretion depends on the cerebral capillary pressure and that this can be easily raised (*a*) by compression of the abdomen, (*b*) by assumption of the horizontal position, and sometimes (c) by forced expiration with the glottis closed, *i.e.* in straining. When, however, the amount of fluid is increased, its chemical characters change, the proportion of solids decreasing.

A. Spina[11] has shown that increased arterial pressure due to intravenous injections of suprarenal extract in curarized dogs causes a clear fluid to exude from the cerebral surface drop by drop. This fluid he considers a transudate. It is probable that the cerebrospinal fluid retains its peculiar characters under normal conditions of pressure only, and after it is withdrawn, its place is taken largely by extraventricular serous transudate.

There are three sources for cerebrospinal fluid, and its character is dependent upon the proportions furnished by the different sources. The first and most important origin is as a secretion into the ventricle from the choroid plexuses; second in importance, as a transudate into the subarachnoid and subdural cavities; and third, from the intraadventitial lymph spaces of the cortex. The relative amount of the intra- and extraventricular fluid varies from time to time, depending on the intravascular and intracranial pressures, a preponderance of the intravascular pressure resulting especially in an increase of the extraventricular fluid. The tension of the cerebrospinal fluid is from 5 to 7.3 mm. of mercury, and about equals that of the blood in the capillaries, varying, however, in different individuals.

The osmotic tension of the cerebrospinal fluid is greater than that of serum (Zanier).

The cerebrum increases in volume with the cardiac systole and expiration, and decreases with the cardiac diastole and inspiration. Accompanying the cerebral movements is an ebb and flow of the cerebrospinal fluid from the cranial into the spinal spaces where extra room can be had by the expansion of the ligaments and the spaces around the spinal nerves. More room may also be had for the brain by the expression of blood from the encephalic veins and sinuses. There is, however, very little motion of translation of the fluid accompaying the cerebral movements (Elder). Whenever the intracranial pressure exceeds the cerebral venous pressure, the fluid rapidly leaks away, and hence may be left out of account in the pathology of compression (Hill).

The effect of intravenous injection of cerebrospinal fluid has been investigated by Mott and Halliburton.[12] They found that if the fluid is taken from animals, or from cases of meningocele or chronic hydrocephalus in man, and injected into the veins of animals, no effect is produced. If, on the contrary, the fluid is obtained from cases of brain atrophy, especially from cases of general paralysis of the insane, then a marked lowering of arterial tension is noticed, partly cardiac in origin but principally due to the local action of the poison on the neuromuscular apparatus of the peripheral vessels, especially in the splanchnic area. This is believed to be due to a toxic substance called cholin derived from the disintegration of the lecithin in the brain.

Chemistry.—There are several ways in which the cerebrospinal fluid may be obtained for examination. (1) From cases of chronic hydrocephalus, either by puncture during life or after death. In acute hydrocephalus the fluid is not normal, but is an exudate. (2) In cases of meningocele and spina bifida the fluid is normal, but only the first tapping can be so considered, as its character changes in the later tappings. (3) By lumbar puncture. (4) The fluid may be collected in cases of fracture at the base of the cranium, as it drops from the nose and ear. (5) In cases of spontaneous flowing from the nose and ear. (6) In animals, by establishing a permanent fistula, as suggested and employed by Cavazzani,[13] to study qualitative and quantitative variations.

The cerebrospinal fluid is a clear watery fluid, slightly saline to the taste, of low specific gravity, about 1.007. The density increases in proportion to the greater amount of transuded to secreted fluid, and it is also higher in the morning than in the evening (Thomson). Its reaction is slightly alkaline or neutral, being more alkaline in the morning than at night. The reaction has been investigated in diseased conditions by Turner,[14] who found in thirty-seven cases of insanity that it was acid to phenolphthalein, alkaline to methyl orange; and in thirty cases tested with litmus there was an amphoteric reaction in

twenty-nine, the red paper finally turning blue, with an acid reaction in one case only. These same reactions were found whether the test was made immediately after death or several hours later. Its cryoscopic point is $-.60°$ C. to $-.65°$ C., but it is somewhat variable and in acute infections approaches that of the blood, $-.56°$ C.

The chemical composition of the cerebrospinal fluid is shown in the following analysis, made by Halliburton,[15] of fluid removed from cases of spina bifida

	Case 1. Female aged nineteen years, in parts per 1,000.	Case 2. Child aged eleven days, first tapping, in parts per 1,000.	Case 3. Child aged thirteen weeks, fourth tapping, in parts per 1,000.
Water	989.75	989.877	991.658
Solids	10.25	10.123	8.342
Proteins	0.842	1.602	0.199
Extractives	9.626	0.631	3.028
Salts		7.890	5.115

A comparison of the relative proportion of solids in several of the watery fluids of the body is shown in the subjoined table (Beaunis):

	Water.	Solids.
Lymph	95.8	4.2
Serum	95.9	4.1
Aqueous humor	98.6	1.4
Tears	98.2	1.8
Cerebrospinal fluid	98.8	1.2

In normal cerebrospinal fluid, proteins are small in amount, and somewhat variable in quantity and kind. Fibrinogen is absent, as no fibrin is formed by the addition of fibrin ferment. Serum albumin is absent, as all of the protein is precipitated by saturation with magnesium sulphate. There are probably present, however, serum globulin, generally protoalbumose, sometimes heteroalbumose, and occasionally peptones. An increase in proteins is likely to occur in tappings subsequent to the first, but never equalling that found in inflammatory hydrocephalus.

The following analysis, in the case of a boy six months old with chronic hydrocephalus, illustrates this (Halliburton[15]):

	Specific gravity.	Protein. Percentages of total proteins.	Protein. Kinds of protein present.	Reducing substance.
First tapping.	1.006	0.045	Globulin. Proto-albumose. Hetero-albumose.	Traces.
Second tapping.	1.010	0.069	Same as first tapping. Serum globulin.	Fairly abundant
Third tapping.	1.010	0.272	Serum albumin. Traces of albumoses.	More abundant.

One of the most interesting features of the chemistry of the cerebrospinal fluid is the presence of a substance which, like sugar, reduces copper salts. It has been considered grape sugar by many observers (Bernard, Cavazzani, Nawratzki,[16] and Panzer[17]).

Nawratzki studied this fluid in the calf, horse, and man. In the calf, working with two liters of fluid, he found a substance which reduces copper and bismuth oxide in alkaline solution, and gives the phenylhydrazin reaction. He obtained crystals having the form and melting-point of phenylglucosazon, 205°–206° C. He failed to find pyrocatechin, peptone, or albumose, and considers the protein a globulin. He claims that the reducing substance disappears shortly after death, and cites two cases in which the fluid drawn by lumbar puncture during life showed strong reducing action, but in the same individuals after death this action was lost. Halliburton always finds the reducing substance, but claims it is not grape sugar for the following reasons: (1) It does not reduce bismuth salts; (2) it does not ferment with yeast; (3) it does not rotate the polarization plane; (4) it does not yield a crystalline compound with phenylhydrazin, as does sugar.

This reducing body can be obtained as follows: "Acidified alcohol is added in excess to the fluid, to precipitate proteins; this is filtered off. The filtrate is evaporated to dryness over a water-bath; the dry residue is again taken up with alcohol, filtered, and again evaporated to dryness" (Halliburton).

The crystalline deposit is the reducing substance and belongs to the aromatic group of organic compounds. It is soluble in ether, alcohol, and water, gives a green coloration with ferric chloride, brown with caustic alkalies, has a pungent taste and an acid reaction, and its crystals are needle-like and similar to those of pyrocatechin. Halliburton considers the reducing substance a normal constituent of the cerebrospinal fluid, contrary to Hoppe-Seyler, who finds it subsequent to the first tapping only. It certainly increases in amount after the first tapping (see analysis). Whether it exists in a combined or an uncombined state is not known.

Some observers have noted an unusual preponderance of potassium salts, but later ones have found the proportion no greater than that of the blood, lymph, or transudates generally. Ferments in the cerebrospinal fluid in health and disease have been studied by Pighini,[21] Kaffka,[22] and Dochez.[23] Proteolytic and diastatic ferments have been described in dementia præcox and dementia paralytica. Lipolytic ferment is found increased in dementia paralytica and cerebral lues. Tryptic and antitryptic ferments are found mostly in dementia paralytica. Oxydases also are present in small amount and perhaps are brought in close relation with the nerve cells by the intracerebral circulation of the fluid. These ferments exist only in small amounts and are not at present of diagnostic significance.

Briefly stated, the chief chemical characteristics of the cerebrospinal fluid are the following: (1) It is a clear watery fluid, faintly alkaline, of low specific gravity, about 1.007. (2) It contains no fibrin and gives no precipitate (mucin) on adding acetic acid. (3) On boiling, not more than a trace of turbidity (serum globulin) is observed. (4) It reduces Fehling's solution. (5) A reducing substance, obtained by evaporating to dryness an alcoholic extract of the fluid, is found in needle-like crystals having a pungent taste and an acid reaction, and resembling pyrocatechin. This reducing substance does not ferment with yeast, nor give the phenylhydrazin reaction, nor turn the polarization plane. (6) It contains a small proportion of proteins and generally no albumin.

Pathological and Clinical Considerations.—Since Quincke called attention to the value of puncture of the vertebral canal as a diagnostic and therapeutic measure, and to the ease with which it could be performed, it has frequently been resorted to.

The method of procedure is as follows: The patient is preferably placed in the recumbent posture on the left side, with the body strongly flexed in the lumbar region. The puncture is made with a long platinum-iridium aspirating needle between the second and third or the third and fourth lumbar vertebræ, a few millimeters outside the median line. In a child of about two years, the puncture should be opposite the mid-point between the lumbar spines, and at a depth of about two centimeters the subarachnoid chamber will be reached. In the adult the puncture should be made at a point just below the end of the spine above, and on account of the downward inclination of the spines, the needle should slope upward and inward toward the median line. If the puncture be made in the median line, it should be at the mid-point between the spines; and, in children the needle should penetrate in a nearly horizontal direction, while in the adult it should slope upward parallel to the spines. Sahli[18] recommends that the puncture be made between the fifth lumbar and the base of the sacrum, especially if the morphological elements are to be sought for. Anesthesia is, as a rule, unnecessary, but an ethyl chlorid spray may be used.

Where there are symptoms of intracranial pressure and only small amounts of fluid can be obtained by puncture, the cause will probably be an interruption of the connection between the encephalic and spinal spaces due to exudate or tumor, especially of the cerebellum. It is possible, however, that the lack of fluid might be due to the closure of the aqueduct of Sylvius or the metapore. Small quantities of fluid exclude tuberculous meningitis, acute hydrocephalus, and tetanus.

The cerebrospinal pressure can be judged by the strength of flow from the cannula, a strong spurt indicating an increased pressure, slow-coming drops a decreased pressure. It can be more accurately measured by attaching the cannula to a mercury, or, better, to a water manometer, the normal pressure being from 5 to 7.3 millimeters, mercury. When the pressure is much raised (fifteen to sixty millimeters of mercury) meningitis or brain tumor is indicated, but variations in pressure are not of much diagnostic value. The specific gravity is somewhat variable, but an increased density points to meningitis, although this affection may exist with normal specific gravity.

Proteins may be found increased in tuberculous meningitis and degenerative diseases of the central nervous system; decreased in brain tumors and serous meningitis. Lichtheim and Quincke claim to find sugar in most cases of brain tumor. This does not agree with the observations of Furbringer, who found sugar only in cases of diabetes associated with tuberculosis. Cholesterin (Pighini[24, 25]) appears as a pathological component of the cerebrospinal fluid and is found increased in degenerative diseases of the central nervous system, as dementia paralytica, severe cases of dementia præcox and epilepsy. Cholesterin is one of the active principles in the cerebrospinal fluid giving the Wassermann reaction. According to some observers, cholesterin may normally exist in the fluid to a slight extent. Cholin is another pathological constituent of the fluid indicative of degenerating nerve tissue and has been found in dementia paralytica by Laignel-Lavastine and Lasausse,[26] who also found in this disease another compound having the peculiarities of trimethylamine.

A turbid appearance is due to leucocytes and indicates inflammation, but in tuberculous meningitis, the fluid is clear.

In tuberculous meningitis, tumor, abscess, and chronic hydrocephalus only a few leucocytes and endothelial cells are to be found, while in acute meningitis the leucocytes are more plentiful, and in the purulent form they are very numerous. It is important, before advising operation in cases of abscess of brain and sinus thrombosis, to exclude purulent meningitis. This is often readily done by a microscopic examination of the puncture fluid.

Pure blood in the subarachnoid space indicates either extensive brain laceration or intraventricular hemorrhages. In subdural hemorrhages, a small amount of blood may be found; but in epidural hematoma, and in hemorrhagic pachymeningitis only very small quantities of blood are found. In severe traumatic cases the presence of nearly pure blood would indicate serious brain injury and contraindicate operation, and *vice versa* the absence of blood might indicate the advisability of an operation. In non-inflammatory diseases of the brain, as tumors or abscess, no clotting occurs, except a slight one in tuberculous meningitis.

In cases in which tuberculous meningitis is suspected, some of the puncture fluid should be centrifugalized and examined for tubercle bacilli. Fürbringer has found the bacilli in thirty out of thirty-seven cases. Other organisms that have been found are the diplococcus intracellularis (Weichselbaum) in cases of epidemic cerebrospinal meningitis, and the streptococcus and the diplococcus pneumoniæ in purulent meningitis secondary to otitis media. The staphylococcus pyogenes aureus and albus are also sometimes found, also B. typhosus, B. coli communis B. pyogenes fœtidus, B. mallei, B. of Neumann-Schäfer and Pfeiffer's influenza bacillus.

St. Clair Thomson has collected from the literature nine cases of undoubted spontaneous flow of the cerebrospinal fluid from the nose, and twelve probable cases. This condition he has named cerebrospinal rhinorrhea. It affects the sexes about equally, and is a disease of adult middle life, frequently presenting cerebral and eye symptoms. The flow is usually from the left side of the nose and is generally continuous day and night, but long or short periods of intermission may occur.

The method of escape of the fluid was found in one case to be through an aperture in the cribriform plate of the ethmoid. A possible explanation is that the lymph vessels of the nasal mucous membrane, which are in communication with the subarachnoid cavity, may furnish the exit. No efficient method of treatment has been found. One case of spontaneous flow from the ear is recorded in which the membrana tympani was intact and no evidence of injury or disease was present.

Diagnosis.—The examination of the cerebrospinal fluid for diagnostic purposes may be conducted in four ways: (1) Bacteriological, (2) chemical, (3) serodiagnosis, (4) cytodiagnosis.

Bacteriological.—The lumbar puncture fluid should be centrifuged and the bacteria identified by staining, culture, and inoculation methods.

Chemical.—Various observers during the past decade have studied the protein content in many diseases. Among these the following may be mentioned: Reichman,[27] Ziveri,[28] Nonne and Holzman,[29] Apelt,[30] Eichelberg and Pfortner,[31] Szécsi,[32, 33, 38] Jach,[34] Franz,[35] Assmann,[36] and Andermack.[37]

The results of these investigators seem to show that the proteins and especially globulin are increased in degenerative diseases of the cerebrospinal system as dementia paralytica, tabes, and cerebrospinal syphilis and is usually accompanied by a lymphocytosis. The total proteins are usually estimated by the Esbach method. For the determination of the globulin the Nonne-Apelt test with ammonium sulphate has been generally used. Szécs,[32] has devised a graduated centrifugalizing tube in which the amount of globulin can be directly read.

Serodiagnosis.—Wassermann's reaction in the cerebrospinal fluid has been studied in various forms of syphilis and metasyphilis by Wolff,[39] Eichelberg,[40] and others. The lipoid and cholesterin in the fluid are believed to furnish the antibodies. In

cerebrospinal syphilis the blood-Wassermann seems less certain and positive than the reaction obtained from the cerebrospinal fluid.

In epidemic cerebrospinal meningitis an aid to diagnosis is found in Vincent's[41] precipitin reaction. This is performed as follows: Centrifuge the cerebrospinal fluid then take three tubes; in one place 100 drops of the fluid, in the second fifty drops, and in the third fifty drops. Add to the first and second tubes one drop of antimeningococcus serum and place in the incubator at 55° C. for eight to twelve hours. If a turbidity occurs in the first and second tubes while the third remains clear the diagnosis is epidemic cerebrospinal meningitis. Louis[42] has substantiated Vincent's conclusion as to the diagnostic value of this precipitin reaction. Also Vincent and Combe[43] have shown that a similar precipitation occurs in tuberculous meningitis when cerebrospinal fluid from this disease is mixed with tuberculin and incubated. It is not possible to diagnose anterior poliomyelitis by serological means (Wollstem[44]).

Cytodiagnosis.—Considerable attention has been given to this subject during the last few years and notable advances made. Among the contributors are Szécsi,[32, 33, 35] Nonne and Holzman,[36] Reichmann,[3] Andermack,[37] Cotton,[45] and Eichelberg and Pförtner[31]. One method of studying the cellular content is by means of smears of the sediment obtained by centrifugalizing the fluid, then fixing and staining with toluidin blue or pyronin-methyl green. A differential count can be made from the smear and the number of cells may be roughly determined by counting the cells in several fields. This is essentially Widal's method and is not considered accurate by most observers.

For the quantitative determination, probably the Fuchs-Rosenthal method or one of its modifications is best. It may be performed as follows: The staining solution is 50 c.c. of a two-per-cent. solution of glacial acetic acid containing 0.1 gram of methyl violet. A mixture is made in the leucocyte-counting pipette by drawing in the staining solution to 0.1 and cerebrospinal fluid to 11. The counting chamber holding 3.2 cubic millimeters is filled and the cells counted, then the $\frac{\text{number of counted cells}}{3.2} \times 1.01$ will equal the number of cells in one cubic millimeter of the fluid. One to five cells are normal, ten cells are distinctly pathological.

For a differential determination of the cells Alzheimer's method is probably the best. The procedure is as follows: 5 or 6 c.c. of cerebrospinal fluid are collected from the needle in a centrifuge tube containing 7 or 8 c.c. of ninety-six-per-cent. alcohol. Then shake and allow several minutes for the coagulum to form; centrifuge at a high rate for one-half hour. Pour off supernatant fluid, dehydrate the coagulum with alcohol, infiltrate, and embed in celloidin and section. Many stains may be used successfully but toluidin blue or Pappenheim's pyronin-methyl green gives excellent results. In making the differential count 300 to 500 cells should be counted, necessitating several sections. Alzheimer's method has been used for quantitative determinations as well, by counting the cells in the immersion fields, but it is not so reliable as the Fuchs-Rosenthal method (Hough[46]).

The following kinds of cells have been described in the cerebrospinal fluid in pathological conditions.

Polymorphonuclear Cells.—These show the usual characters of the leucocyte except that the cytoplasm frequently does not stain so readily and the granules are usually absent; eosinophiles may also occur. They are increased especially in acute meningitis.

Small Mononuclear or Lymphocytes.—These are similar to ordinary lymphocytes, but occasionally the cytoplasm is lacking, or is irregular, or mostly on one side. These are the most numerous of all the cellular elements in chronic inflammation of the meninges and are likewise increased in dementia paralytica, tabes, and cerebrospinal syphilis.

Large Mononuclear.—These cells resemble somewhat large mononuclear leucocytes, but the nucleus is more irregular and eccentric. They are phagocytic and found mostly in dementia paralytica and cerebrospinal syphilis. Their origin is not certainly known.

Macrophages.—These cells have somewhat the appearance of the large mononuclear, but are greater in size, with the nucleus frequently near the periphery; they contain included cells or other substances and are actively phagocytic. They may arise from the large mononuclear and they have the same significance.

Endothelial Cells.—These probably come from the meninges, their nuclei are oval, the cytoplasm small in amount, and they are found mostly in dementia paralytica and cerebrospinal syphilis.

Körchenzellen.—They are large round cells with lightly staining nuclei at the periphery, the cytoplasm contains globules probably of a fatty nature, and they are found in dementia paralytica and other degenerative conditions of the central nervous system and may be modifications of the large mononuclear cells.

Plasma Cells.—These cells are of moderate size and rounded with a single and often eccentric nucleus. The cytoplasm is usually deep staining and granular. Possibly they are derived from the lymphocytes, but more probably they come from the pia as similar cells are found there. They are present chiefly in dementia paralytica, but are not pathognomic of that condition.

Fibroblasts are small slender cells with elongated nuclei and are of unknown origin and significance.

Ependymal cells are small cells with spherical nuclei with little or no cytoplasm, found mostly in postmortem fluid and may possibly be shed cells of the ependyma. According to Hough[46] protagon granules may sometimes be found in the fluid.

In general, increased proteins, globulin, and a pleocytosis especially of the lymphocytes indicate degenerative diseases of the cerebrospinal system as opposed to functional neuroses. No kind of a cell is pathognomic of any disease (Jach[34]) and lymphocytosis in the cerebrospinal fluid is not parallel with that of the blood. Apelt[47] has shown that in trypanosomiasis in dogs the cerebrospinal fluid shows an increase of proteins, globulin, and a lymphocytosis as well as the presence of the trypanosomes. Martin and Leboeuf[48] have found that a lymphocytosis likewise occurs in man.

HARRY B. FERRIS.

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Cerebrospinal Meningitis, Epidemic.—See under *Meningitis.*

Cerebrin.—See *Cerebrosides.*

Cerebron.—See *Cerebrosides.*

Cerebrosides are nitrogenous substances free from phosphorus which on boiling with dilute mineral acids yield a reducing substance which has been identified as galactose. From their resemblance to glucosides on treatment with acid has been derived the term cerebrosides. These compounds are found in nervous tissue in comparative abundance. Those that have received recognition as chemical entities are cerebrin, cerebron, kerasin, and encephalin. It is probable that the same body of varying purity has been isolated at times and given a new name. The substances pyosin and pyogenin isolated from pus also belong to the cerebrosides. The cerebrosides have solubilities similar to those of the fats.

FRANK P. UNDERHILL.

Cerium.—A single salt, only, of cerium is official in the United States Pharmacopœia, namely, cerium oxalate, entitled *Cerii Oxalas.* This salt is "a fine white powder, without odor or taste, and permanent in the air. Insoluble in water, alcohol, ether, or in solutions of potassium or sodium hydroxide; insoluble in cold, but soluble in hot diluted sulphuric or hydrochloric acid." (U. S. P.) In effect cerium oxalate resembles the insoluble bismuth compounds, being, from its insolubility, devoid of active properties, but yet like many other insoluble metallic powders, having a power to allay local nervous irritability, This influence is utilized to combat reflex nausea and vomiting, especially the vomiting of pregnancy, and also to repress irritative dry coughs. In this latter application, when successful, the present drug has the advantage over the ordinary run of cough medicines of not disordering the stomach, but, on the contrary, of tending to quell any irritation of that organ. The oxalate may be given in doses of gr. v. to x. (0.3–0.6) several times a day, best taken dry upon the tongue. Such doses may be kept up for a number of days in succession with no other effect than causing, at first, a little dryness of the mouth. For cough, the medicine should be persisted in even if, as may happen, there be no benefit for the first two or three days; and especially should doses be given on the empty stomach early in the morning and late at night. The pharmacopœial dose of one grain is eminently safe; but it is doubtful if it is accompanied by any beneficial result.

EDWARD CURTIS.
R. J. E. SCOTT.

Cerumen is the mixture of substances contained in the secretions of the sebaceous and sweat glands of the outer passages of the ear. In it may be found soaps and fats, protein, fatty acids, cholesterol, and a red alcohol-soluble body with a bitter sweet taste.

F. P. U.

Cervical Ribs.—A cervical rib is a congenital error of development, an evidence of atavism, char-

acterized by unusual development of the anterior tubercle of the transverse process of the seventh cervical vertebra. Such ribs may vary from mere nodules to full ribs that are attached to the manubrium through their cartilage. They usually arise from the anterior tubercle of the transverse process, the so-called costal process; they sometimes arise from the body of the vertebra or from the intervertebral disk. The vertebral attachment may be either with or without an articulation.

The following forms of cervical ribs may be recognized: (1) Rudimentary, simply a projection from the body of the vertebra. (2) An inch or so in length and free. (3) Apparently connected by means of a ligament to the first rib. (4) Articulating directly with the first thoracic rib.

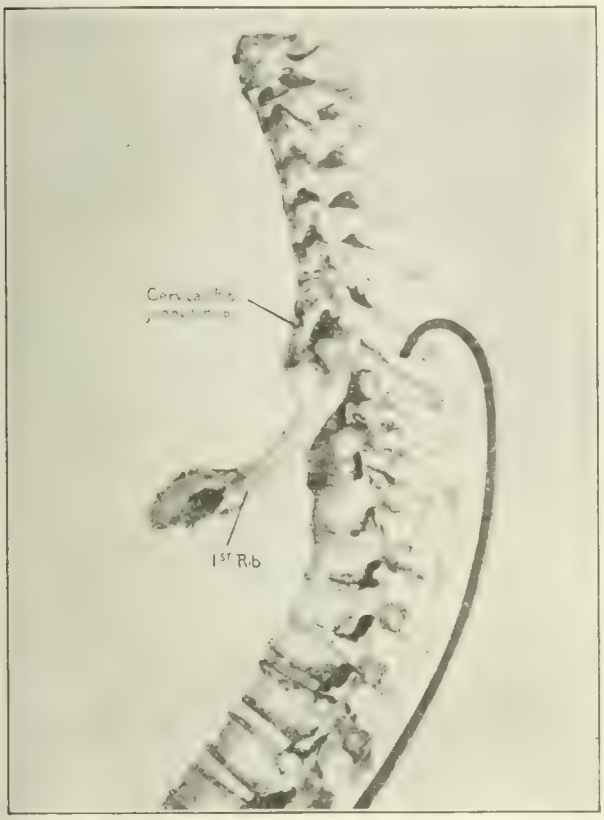


Fig. 1362.—Cervical Rib. (Elder, Text-book of Anatomy, Museum, McGill University, Montreal.) Note deformed first rib.

Gruber gives the following classification of cervical ribs:

First degree: marked by only a slight increase of the costal process, not reaching beyond the true transverse process.

Second degree: protruding beyond the transverse process, ending free or attached to the first rib.

Third degree: marked by a complete body, extending approximately to the cartilage of the first rib, being united to the cartilage directly or by means of a ligament.

Fourth degree: a complete cervical rib, attached to the manubrium through the cartilage of the first rib.

Cervical ribs have been known as postmortem curiosities since the time of Galen. With the advent of radiography, the literature began to teem with reports of cases in which the diagnosis was made during life.

The age at which the defect is recognized has varied, in the reported cases, from the fetus of six months to advanced life. Symptoms usually do not appear until adolescence or later. From the reported cases, this anomaly seems to show a decided preference for the female sex, the proportion being about 3:1. This may be because the neck of the female is more commonly subjected to scrutiny and examination.

Pilling, in 1894, from a study of 139 cases collected from the literature up to that time, believed the affection to be bilateral in about two-thirds of the cases. Radiography has shown the fallacy of this view, which seems to have been entertained because only the larger rib produces symptoms, the smaller rib on the opposite side being frequently overlooked. It is rare that symptoms have been recorded upon both sides.

Anatomical Relations.—In two of the cases (Struthers and Ehrich) two ribs were found on one side, arising from the sixth and seventh cervical vertebræ. Several other cases of cervical ribs arising from the sixth cervical vertebra have been reported, but are open to doubt. In Czerny's case, a lipoma was removed from the neck, the pedicle of the tumor being a cervical rib attached to the fifth cervical vertebra. These are mentioned rather as curiosities. Almost invariably the cervical ribs arise from the seventh cervical vertebra.

Halbertsma declared that when the length of the rib is under 5.1 centimeters the artery passes in front, but when the length is 5.6 centimeters or more the artery passes over it. This is apparently the rule, though there are many exceptions to it. It would seem that the artery never runs under the cervical rib, so that in these cases the artery is always more accessible for compression than in the normal individual. The vein is in front of and below the artery, so placed that it is not compressed between the cervical rib and the scalenus anticus. Therefore, these cases usually do not show edema of the arm.

The brachial plexus accompanies the subclavian artery, above and to the outer side. Therefore, in the removal of a cervical rib, it is usually practicable to displace the brachial plexus upward and outward, and the artery downward and inward.

If the cervical rib is well developed, an intercostal muscle, usually the external one, may be present. The scalenus anticus may be inserted into the anterior extremity of the rib. Sometimes the scalenus medius and posticus are also attached to the well developed rib, occasionally the artery and nerve penetrating the former.

The pleura is described as arising higher up in the neck in these cases, though it is not encountered in some cases in the operation of removal of the rib. On the other hand, the pleura may be firmly adherent to a cervical rib.

Symptoms.—These are conveniently classified as local, nervous, vascular, and muscular symptoms.

Local Symptoms.—The tumor in the neck is usually both palpable and visible an inch or so above the middle of the clavicle. Upon palpation we find a rounded hard mass, sometimes movable, more often immovable. The mass extends back toward the seventh cervical vertebra. Above the mass, running downward and outward may be felt and sometimes seen the pulsating subclavian artery. Above and to the outer side of this vessel is the brachial plexus, a region marked by tenderness.

Nervous Symptoms.—These are present in about two-thirds of the cases. Shooting pains radiate from the neck down the arm, sometimes as far as the elbow, possibly to the hand, following the ulnar more often than the radial side of the forearm. Less often the

pain radiates to the head or to the chest. Sometimes it begins in the fingers and extends upward. The pain is often attributed to hard work or muscular exercise by the patient, and is said in some cases to be worse in winter than in summer.

Often there is anesthesia, more or less complete. More frequently there is paresthesia, such as tingling, formication, and numbness.

Depending upon the degree of injury of the nerve, there may be alterations in the electrical reaction, advanced cases showing the reaction of degeneration.

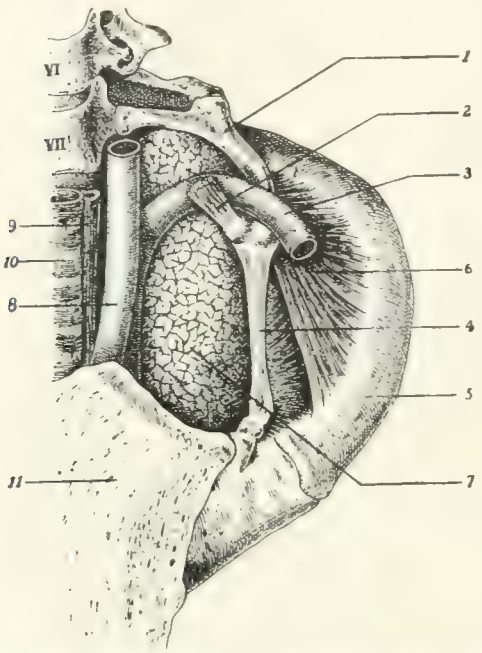


Fig. 1303.—Rudimentary Rib in its Relations to Surrounding Parts. (From Luschka.) 1, Rudimentary rib with its knobbed end, to which is attached the scalenus anticus, 2; 3, subclavian artery; 4, ligamentous cord, by which the rib is prolonged to the sternum; 5, first dorsal rib; 6, intercostal muscle between the cervical rib and the first dorsal rib; 7, the lung; 8, left carotid artery; 9, esophagus; 10, trachea; 11, sternum. Note the relation of the pleura and lung to the cervical rib.

Affection of the sympathetic nerve has been observed frequently. Thus, there may be profuse sweating and coldness on one side with dryness of the skin on the other; rapid pulse due to irritation of the sympathetic; possibly dilatation of the pupil. Hoarseness has been observed in some cases, and in at least one case there was paralysis of the right vocal cord. However, that was a case showing syringomyelia, which seems to be not uncommon in cases showing this defect in development.

Vascular Symptoms.—Pulsations of the subclavian artery, to which we have referred, may be absent, the artery in some cases being converted into an impermeable cord, probably through thrombus or aneurysm. Therefore, it is not surprising that the radial pulse is often absent. The resulting ischemia causes the hand to become cold, blanched, possibly blue, resembling much the picture observed in Raynaud's disease. Gangrene, however, is not common, because of the establishment of more or less complete collateral circulation. The thrombus may extend upward to the subclavian. In the rare cases in which gangrene supervenes, it involves the tips of the fingers and does not extend above the first phalanx. In this connection, it may be remarked that raising the arm favors the circulation and tends to lessen pain. Edema is usually absent.

The subclavian artery is sometimes found enlarged at operation, but aneurysm is probably much less common than the clinical records would indicate.

In the cases of aneurysm observed by Adams and Keen, the dilatation of the vessel occurred *distal* to the cervical rib and scalenus anticus muscle (Fig. 1304). Bruit or thrill, one or both, may be present. The bruit is not propagated and tends to disappear when the arm is raised. It is doubtful whether these dilatations of the subclavian artery are true aneurysms.

Muscular Symptoms.—Both the muscular and sensory symptoms seem to indicate involvement of the lower cords of the brachial plexus. Wasting of the muscles leads to a diminution of the circumference of the arm and forearm on the affected side from one to four centimeters. The atrophy of the thenar, hypothenar, and interossei muscles is often apparent. The patient tires more readily on the affected side, and there is more or less interference with the more delicate movements, observable especially in writing, sewing, etc. Dysphagia has been mentioned in a number of cases, but seems to be hysterical in nature.

Scoliosis is remarkably common in cases of cervical rib, the convexity being usually toward the larger cervical rib.

Diagnosis.—As is true in the diagnosis of many conditions met by the physician and surgeon, much depends upon the readiness with which we suspect the existence of the malady. It is usually easy enough to confirm or disprove a tentative diagnosis, once our suspicion is aroused. And so it is in the cases of cervical rib. Here the tentative diagnosis is readily proven true or false by resort to radiography. The

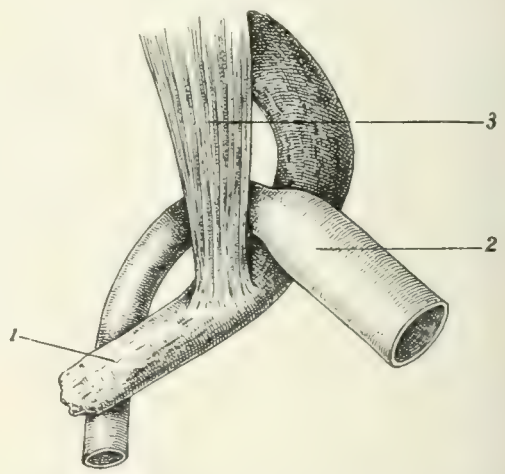


Fig. 1304.—Rudimentary Rib. (Case of Dr. W. W. Keen.) 1, Cervical rib; 2, subclavian artery; 3, scalenus anticus muscle. Note the marked increase in size of the subclavian artery after escaping from behind the scalenus anticus. (Am. Practice of Surgery.)

presence of the characteristic tumor, with the presence of more or less of the vascular, nervous, and muscular manifestations of the affection, to which we have referred, should lead to the suspicion of the presence of a cervical rib, when radiography will make the diagnosis.

Radiographs are sometimes misleading. Two of the leading *x*-ray experts of Berlin are reported to have been misled by the radiographs of conspicuous lateral processes of the seventh cervical vertebra. At any rate, it is safer for the radiograph of such a case to be made and interpreted by one familiar with this work.

Prognosis.—Often there is an entire absence of symptoms, the welfare of the patient being apparently unaffected by the presence of the anomaly. The presence of vascular, nervous, or muscular symptoms, indicative of injury to the brachial plexus or the subclavian artery, may sometimes be relieved, at least temporarily, by so-called medical means, more especially rest with the arm raised, massage, and electricity. However, after the development of such symptoms, the result of treatment is usually not satisfactory unless the offending rib is removed. When required, the earlier this operative procedure is resorted to, the better is the outlook regarding the restoration of function of both the nerve plexus and artery.

Treatment.—The treatment is essentially operative, the removal of the offending cervical rib, in cases presenting marked symptoms. The operation is done under aseptic precautions, such as all modern cutting operations entail. The incision may be made parallel with the clavicle, or vertical, between the sternocleidomastoid and the trapezius. The latter is preferable for long thin necks, the latter for a stout neck of medium length. Often a combination of these two incisions is more satisfactory. At any rate, the incision should be such as to give ample room. The pleura may or may not be encountered. The cervical rib is then exposed by blunt dissection, the intervening vessels being double ligated and divided. The rib is then freed from any attached muscles and isolated by careful dissection. Sometimes the dome of the pleura is attached to the rib. The brachial plexus is drawn outward and upward, the subclavian artery downward and inward.

No careful surgeon would thus injure the artery, but a number have dragged upon the brachial plexus to such a degree as to produce severe pain for several days. This may be necessary but usually may be avoided. The exposed rib is then removed as far backward and forward as necessary and the remaining stumps rounded off. Ordinarily the wound is closed without drainage, depending largely upon the operator's confidence in his asepsis. Tears in the pleura are of no consequence if immediately closed, avoiding the entrance of air, kept free from infection, and promptly repaired.

After removal of a cervical rib, as described, union occurs in a few days. In the way of after-treatment, massage, electricity, and active and passive movements are of value in the restoration of function.

George E. Malsbary.

Cesarean Section.—Cesarean section is a term used for operations which remove a fetus from the uterus through the abdominal wall, the peritoneal cavity being opened in all cases. Historically it is one of the oldest of obstetrical operations recorded.

It is generally supposed to have received its name from Cæsar, who was believed to have been born by abdominal section. But, whether this be true or not, it was performed many years before his time. Furthermore, the name, according to Pliny, was derived from the Latin *cædere*, "to cut," which makes the term cesarean section rather meaningless and the use of the capital C inappropriate, but usage gives it a definite meaning and place.

Until the Middle Ages the operation was largely performed only to deliver a child when the mother was dying. The Roman laws forbade the burial of a pregnant woman until the child had been removed. The first performance of the operation on a living woman which is recorded was in 1500 A.D., the operator being a butcher named Jacob Nufer, in Switzerland. In Germany, Trautmann, of Wittenberg, inaugurated the procedure in the year 1610. The patient lived three weeks.

Until the advent of antiseptic surgery in recent times the mortality following the operation was too great to encourage its employment in any but extreme circumstances.

Until the introduction of recent modifications the various steps in the operation were: 1. Section of the abdominal wall, usually in the median line between the pubes and umbilicus. 2. Section of the uterus *in situ*, the incision being made upon the middle, anterior surface from above downward. 3. Removal of the child and placenta. 4. In some cases suturing of the uterine wound, and in others leaving it to close by general contraction of the uterus; and suturing of the abdominal wound.

The three improvements that have brought the mortality of cesarean section from nearly one hundred per cent. to about five per cent. are: antisepsis and asepsis; complete muscular and serous suturing; coaptation in the uterine wound; operation at the selected time, instead of when patients were mostly moribund, or exhausted by long labors; and the Porro hysterectomy.

Methods of Operating. Sänger's name has been given to *Celiohysterotomy* (the Sänger operation). The simple celiohysterotomy form of cesarean section. For performing this operation the patient is prepared as for any abdominal section. The urine should be carefully tested, the bowels thoroughly emptied, the abdomen washed with green soap and tincture of iodine. The pubes should be shaved, and the vulva and vagina made as aseptic as possible. This latter is best accomplished by first douching with hot bichloride solution and by dusting boric-acid powder into all the crevices of the introitus vaginæ and the vulva. The urine should after this be drawn with a soft catheter. The instruments needed are: scalpels, two mouse-toothed dissecting forceps, one dozen artery forceps, scissors, long-curved needles, as well as some that are small and short, needle-holders, sutures of medium-sized silk, silkworm gut, and catgut; two pieces of either solid rubber ligatures or tubing, each about eighteen inches long; several pedicle clamps; right and left aneurysm needles, and one large vulsella forceps.

When to Operate.—There are some advantages in operating when the patient is in labor, the choice moment being when the uterus is awakened to active rhythmic pains, but previous to any exhaustion.

There is less liability to failure of the uterus to contract after section and removal of its contents. The cervix is also more succulent, and will permit delivery of the placenta *per vias naturales* if that proves best. On the other hand, it is difficult to make as thorough preparation for operation and perform it before any exhaustion of the patient occurs, if the time is decided by the occurrence of labor, which may be at an inconvenient hour. Generally, when the operation has already been decided upon, the operator selects his time. This time should, of course, be as near term as possible, unless there are special indications to the contrary.

Steps of the Operation.—The abdominal incision is made in the median line, running from one inch and a half below the umbilicus to just above the pubes, or in the median line above the umbilicus (Bar's incision). Inasmuch as incision of the uterus at the upper instead of middle anterior part is now most in favor, the high abdominal incision is preferable. With the use of iodine for sterilizing the abdominal wall, care is needed to prevent contact of the intestines with the skin, lest the iodine provoke postoperative intestinal adhesions. Usually the uterus lies in contact with the abdominal wall, the omentum and intestines being above and somewhat to the left of that organ, but it is not wise to assume this and cut at one stroke through the abdominal wall. There is no need of such effort at speed.

There are at this stage two methods of handling the uterus: one to incise it *in situ*, and the other to lift it out of the abdominal cavity and then incise it. The first method can be used when the uterus is free from infection and the fetus of moderate size. It has the advantage of requiring less length of incision in the abdominal wall than the second method, and of causing less exposure and displacement of the intestines. The second method has the advantage of more thoroughly keeping the fluids from the uterus out of the abdominal cavity, and permits better control of uterine hemorrhage. There are also two methods employed for the control of hemorrhage. By one the uterus is constricted by means of a rubber ligature (this is about one-eighth of an inch thick and eighteen inches long), or by rubber tubing, which is passed around the lower portion of the uterus, and either tied tight with the knot in front, or a single turn in the knot is made and constriction applied according to the need during the operation. By the other method an assistant grasps the lateral attachments of the uterus with the thumbs and fingers of both hands and makes compression of the uterine and ovarian arteries as required. The advantages of the rubber constrictor are: that it does not require an individual assistant, that it more surely prevents hemorrhage, and that it is less in the way of the operator than are the hands of an assistant. It has a distinct disadvantage in its liability to cause asphyxiation of the child; and it has a tendency to cause partial paralysis of the uterus, and so favors bleeding by preventing uterine contraction after the organ is emptied. A good assistant holding the uterus can both estimate the degree of compression required and apply it with lessened liability of fetal asphyxiation. He can also be of service in steadying the uterus for the operator.

The uterine incision should be a clean cut, which should be made at first only large enough to admit two fingers, when the opening can then be enlarged with the fingers holding it open, and either a bistoury or blunt scissors used for making the enlargement.

Many different incisions of the uterus have been advocated, but only one—the longitudinal—can be employed with the uterus *in situ*. Following is a list of the various incisions advocated: the longitudinal middle third (Sänger); the posterior surface (Cohnstein); the transverse lower segment (Kehrer); the transverse fundal (Fritsch); the sagittal fundal (Müller-Caruso); and the longitudinal, from fundus to Bandl's ring (Bar). Originality has evidently found its limit in methods of making uterine incision; even the cervical incision of the discarded laparoelytrotomy is excluded from the pioneer.

Of the above methods only those of Bar, Sänger, and Fritsch need to be considered. The Sänger incision is not rightfully his, as it was performed long before his time. The choice between it and that of Bar would depend largely upon the location of the placenta, if that could be determined—which it usually cannot. There is less certainty of contraction of the lower portion of the uterus, which gives Bar's incision an advantage for securing both greater avoidance of hemorrhage and better behavior of the wound when sutured. It is claimed for Fritsch's transverse incision that there is less hemorrhage than in the longitudinal incision because the uterine vessels pursue a transverse course; also that there is least liability of finding the placenta in this region. Neither of these views has any special foundation in fact. It might be claimed for the method that the risk of infection is lessened by having the line of incision run at right angles to the abdominal incision, whereby possible infection of the latter would be less liable to come in contact with the former. Hahn, in 1889, gave a summary of a total of fifty-one cases of cesarean section performed by Fritsch's method up to date. Two died, both from circumscribed peritonitis. The summary is inconclusive so far as showing any special advantage over Bar's incision. In the absence of special indications, Bar's incision is best.

While the uterus is being incised an assistant should endeavor to keep the lips of the abdominal wound closely coaptated to the uterus to prevent the entrance of fluids into the abdominal cavity.

There are certain advantages in bringing the uterus out of the abdominal cavity before incising it, and likewise disadvantages. The advantages are: the uterus can be better handled, its contents can be kept out of the abdominal cavity, and some time can be saved. The disadvantages are: the long abdominal incision, and the greater liability to hernia and to adhesions.

The disadvantages are subject to control by perfect technique, so that the well-known surgical rule can be applied, that free incision with perfect technique appeals to first-class operators as against the opposite method. The method with the uterus brought out should always be selected when there is any suspicion of an infected uterine cavity.

The length of the incision of the abdominal wall can best be determined in each case. Before drawing the fundus out of its bed it is well to pass two long sutures through the upper abdominal wound. These can be used, after removal of the uterus from its bed, to hold the intestines back in place. When the uterus is drawn out it should be covered with warm, sterile cloths. Pads or mats of sterile gauze should be packed underneath, to protect the abdominal cavity from fluids. In cases of special sepsis, in which it is necessary to incise the uterus before ablating it in order to save the child, it is a good measure to slip a large sheet of pure rubber, properly sterilized and punctured, over the entire uterus down to the cervical portion. It will automatically keep out every drop of fluid from the cavity.

Location of the Placenta.—As the result of unusual opportunity and very careful observation, G. Leopold has been able to formulate a rule for determining the placental site when the uterus has been brought into view by abdominal section. There is a constant relation between the placental site and the direction of the tubes, the latter extending backward when the after-birth is on the anterior wall, and remaining laterally, or rather directed forward, when it is on the posterior wall. In some cases there is a bulging of the uterus over the site occupied by the placenta. These are means of diagnosis which come within reach when the uterus has been exposed by abdominal section, and which can therefore be utilized in cesarean section. If the placenta were thus indicated as being upon the anterior middle surface of the uterus, it would be well to make the incision transversely across the fundus (Fritsch's incision), or transversely across the posterior fundus (Cohnstein's).

In making the incision through the uterus the placenta must be disregarded once the incision has been started. It can either be cut through, or separated if its edge is near the wound. The wound being of sufficient size, the child is drawn out either head or foot first, whichever way proves most convenient. The placenta may then either be removed through the opening or, the cord dropped back within the womb, be extracted through the cervix.

In the treatment of the uterine wound it is only a matter of historical interest that it was formerly thought unnecessary to suture this wound. It was thought that the uterus, being a contracting compound of variously running muscular fibers, would close the wound without the assistance of any sutures; but this view has been found to be altogether wrong, and no further discussion of it is permissible. The opposite treatment, that of water-tight suturing of the wound, is now altogether employed.

To get the most absolute coaptation and impervious union of the lips of the wound, Sänger went to the

extreme of advocating the dissection of a thin strip of muscle from each raw surface of the wound in order that the peritoneum could be enfolded on both sides and prompt sealing of the wound by peritoneal agglutination thereby secured. Even this time-taking and troublesome dissection has already become historical. It is found correct in aim, but entirely unnecessary, as the same degree of coaptation can be secured by enfolding superficial sutures.

It should be borne in mind that perfect closure of the uterine wound is essential to success, and the method employed should not be slighted by any one.

First, a row of deep sutures of silk should be inserted, extensive enough to include the muscle, but not the endometrium or decidua. These sutures should be placed—interruptedly—about 1.5 centimeter (3/5 inch) apart, and should emerge at the same distance from the edges of the wound. Between these should be inserted a similar series of sutures at half the depth of the first set. In inserting these sutures care should be taken to have the opposite surfaces meet without irregularity in spacing, lest wrinkling result and afford a pocket for infected secretion. As the uterus will sustain constant rhythmical contractions and relaxations, it is well to tie the sutures a little too tightly rather than too loosely. A slight blanching of the included tissues is evidence of proper tension by the sutures. When both layers of the deep and half-deep sutures have been tied, a superficial row which includes only the peritoneum should be introduced. These are intended to enfold the peritoneum and bury the other sutures. Fine silk should be used. These sutures include just enough peritoneum to secure a good hold, and run entirely over the deeper layers. They may be either interrupted or continuous, following the method of Lembert in suturing the intestine. The latter method is quite as effective as interrupted suturing, and has the advantage of saving time.

As in every abdominal operation, very careful cleansing of all parts by gauze sponging should be employed, the region behind the uterus receiving special attention. Hunter Robb advises drawing the omentum down behind instead of in front of the uterus in making the final toilet of the abdominal cavity, as proving less likely to cause omental adhesions and subsequent hypogastric and epigastric pains after the uterus has contracted.

In removing the placenta, it is possible, with a little care, to avoid bringing the hands in contact with the uterine wall by keeping them within the amnion, the placenta being grasped on its fetal surface with the amnion entirely enveloping the hands.

Irrigation of the uterus after section is not usually indicated, inasmuch as this method of operating should not be performed if infection has already taken place, the Porro method being employed instead. There may be circumstances present in the operation interfering with perfect asepsis, in which case thorough douching with bichloride solution—1 to 10,000—should be employed.

In the after-treatment of the patient but little variation from ordinary management in abdominal operations is indicated. If the bowels were not properly—*i.e.* thoroughly—emptied previous to operation (this is peculiarly liable to be the case in cesarean section, where so many cases are emergency operations), efforts should be made to secure thorough cleansing at once. Otherwise the second day will be best for the administration of cathartics.

The vagina should be douched after operation to remove blood accumulations, and then treated as in ordinary labors in which douching is not necessary; but careful dressing of the vulva with sterile gauze and cotton pads is essential. Voluntary micturition is preferable to catheterization. There is a physiological advantage in placing the child to the breast at regular intervals, as this stimulates the uterus to healthy contraction and favors involution. The patient should not be asked, however, to feed the child from the breasts, unless she is quite able to do so without feeling the drain.

The patient should be allowed partially to sit up in bed after eight or nine days, according to the conditions. To avoid abdominal hernia, it is best not to hurry getting the patient on her feet, the fourth week being usually time enough. An abdominal bandage, or truss, should be worn for a while.

Celiohysterectomy (the Porro operation).—In 1876 a modification of the classical cesarean section was performed by Edward Porro, which consisted in ligation of the uterine and ovarian arteries and removal of the uterus at the cervix, the stump being brought into the abdominal wound and there fixed.

There are two methods of performing this operation: one, the original Porro method, in which the same steps are taken, as in the method just described, up to the removal of the child, after which the ovarian and uterine arteries in the broad ligaments are tied, and the uterus is then cut away just above the ligature; and the other known as the Porro-Müller method, in which the abdominal incision is made sufficiently large to permit bringing the uterus out of the abdominal cavity before removing the child, when the latter, if still alive, is removed by opening the uterus; or if the child is dead, or the uterus is dangerously septic, the entire uterus is cut away without opening it.

When the Porro method—removal of the uterine contents with the uterus *in situ*—is employed, great care is necessary to prevent contact of any of the uterine fluids with the abdominal cavity, inasmuch as this operation is generally done in preference to the so-called Sänger operation because the uterus is believed to be septic. It is better, when doing the operation, to ligate the neck of the uterus more tightly than is done in the Sänger operation, as it is most desirable to avoid flowing into the abdominal cavity, while there is no need of preserving uterine tonicity.

In doing this operation there is no necessity for care in making the opening into the uterus, and it is permissible to tear the opening with the hand instead of cutting to the desired size with knife or scissors. This may save some time and lessen hemorrhage. It is also well to draw a pad of sterile gauze down behind the uterus before making the incision into it. This will best prevent the entrance of fluids into the abdominal cavity. After the uterus has been emptied it should be cut away with scissors at about one inch above the line of constriction, the tubes and ovaries being included. The vessels should then be ligated, including those in the stump. The raw surface of the stump is next seared with pure carbolic acid. The abdominal wound is then sutured down to the stump. Knitting needles, or pins six inches or more in length, are passed through the stump, including the ligature, and are protected from cutting into the abdominal wall by pads of gutta-percha or closely folded gauze. The stump is generally well dusted with iodoform and boric-acid powders, though there is a developing tendency to discard iodoform at the present time. The entire wound is then covered with sterile gauze pads and absorbent cotton. These dressings may require removal and fresh ones to be put in their place in two or three days, especially if sepsis develops in the stump.

A modification of this method of treating the stump is known as the subperitoneal method, in which, instead of bringing the stump into the abdominal wound and fixing it there, it is left *in situ*, and a layer of peritoneum from the posterior surface of the lower uterus is dissected free from the uterus before the constrictor is applied, and then closely stitched over the stump to the peritoneum in front. This method requires, in place of the constriction ligature around the neck of the uterus, the application of clamps to the vessels in the broad ligaments; then, after removal of the

uterine contents, the peritoneal flaps are dissected loose. The constrictor can then be applied without involving the flaps. This method requires more time than the older one, but is preferable when feasible.

Complete Hysterectomy.—The removal of the entire uterus and cervix is necessary in conditions such as cancer involving the cervix. When this is done, instead of ligaturing the stump the vessels are tied in the broad ligament and the uterus dissected out complete, as in ordinary hysterectomies in gynecological work.

Indications for Cesarean Section.—Certain cases of pregnancy are met with in which the physician has the choice of only one method of relief—cesarean section.

Tumors and Diseases.—Tumors of the lower segment of the uterus which cannot be removed by vaginal operation, and which are of such size as to prevent dilatation of the cervix sufficient to permit passage of the fetus, necessitate celiohysterotomy. Fibroids are most frequent in this list. Ovarian tumors impacted in advance of the head, and occupying the pelvic basin to the obstruction of the fetus; rarely a dislocated and adherent kidney; intestinal displacement; carcinomata of the cervix, rectum, sigmoid flexure, and vagina, and certain obstructive growths following old cases of appendicitis, compose most of the abnormalities necessitating cesarean section. Exostoses may also compel the operation. Cicatrices of the vagina may be of sufficient size to compel cesarean section. It is not worth while to classify some of these obstructions as "absolute" indicators of cesarean section, because every case offers an individual equation, and must be decided by itself.

It may be that slitting the cervix in some cases of tumor, such as myoma, will be less dangerous than cesarean section; or a tumor of the ovary prolapsed into the pelvis may be removed with less danger than a cesarean section involves. In tumors of the lower uterus the imminent danger of rupture of that organ in cervical dilatation must be given much weight. In cicatrices of the vagina it may seem feasible to cut and dilate them, but they are liable to tear much beyond safe limits in the passage of the fetus.

In all these various indications the general rule prevails among experienced operators that a controllable operation like cesarean section is much safer than severe straining and mashing of tissue involved in drawing a fetal body through an abnormally obstructed vagina. Incisions of the cervix or of vaginal cicatrices, with blind traction and distention, cannot equal aseptic, clean abdominal incisions and neat suturing of wounds, even though the latter be great in extent.

Pelvic Contraction and Large Head.—When a pelvis is too small to allow passage of the head of the fetus by symphyseotomy or pubiotomy, or when craniotomy would be as difficult and dangerous as a cesarean section, the indications for the latter operation may be classed as absolute. But it is almost useless to define such conditions by fixed pelvic diameters. A conjugata vera of but two inches would be "absolute," but between two and one-half and three inches it is not possible to classify the indications. The only proper method of determining the dimension indications for cesarean section is to learn the relative proportions existing between fetal head and pelvic caliber; and pelvic measurement is only one-half of the problem.

Contraction of the pelvic canal of sufficient degree to render craniotomy as dangerous as cesarean section is one of the rarest abnormalities in obstetrics. The degree of contraction which renders the operation of symphyseotomy or pubiotomy out of the question should be determined. This method of delivery occupies a field limited to such degree of disproportion as will permit passage of the fetal head after section of the pubic joint or ramus without necessitating a separation of the pubic bones of more than two and three-fourth inches. A greater separation of these bones involves such risk to the sacroiliac joints and the vaginal wall and bladder as to condemn either operation. Cesarean section should be the absolute choice in such cases. Symphyseotomy or pubiotomy should be performed only when the patient is in labor, and the most useful and the safest method of determining how much separation of the pubic bone would be required is direct palpation of the head and pelvic inlet with the hand in the vagina. Approximately indicating by figures the limits, we would state that a conjugata vera of three inches and a fetal biparietal diameter of from three and one-half to four inches would not cause too great separation of the pubic joint. Wotherspoon delivered a child weighing fifteen and one-half pounds with a separation of nearly five inches; and the patient recovered, but with a torn vagina, urethral fistula, and one-half of an inch separation of the pubic bones. Such cases get beyond the control of the operator, and are not justifiable when foreseen.

The comparative mortality and morbidity of cesarean section, induced labor, symphyseotomy, and pubiotomy depend, in the answer, upon many variable points. Induced premature labor is safest for the mother and most dangerous for the child in cases requiring delivery before the thirty-second week. Cesarean section is most dangerous for the mother and safest for the child; symphyseotomy and pubiotomy are safer for the mother than cesarean section, and somewhat more dangerous than induced premature delivery. They are less dangerous for the child than the latter method, and more so than is cesarean section.

The essential operative mortality (that percentage of fatalities which will follow the surgical work of the best operators in cases taken at the time most favorable, and which must follow present methods of performance in these several ways of delivery) must be the foundation for selection of method.

Induced premature labor for dystocia is essentially always of the above class, as it is performed voluntarily and at the convenience of operator and patient. The mortality is about four per cent., but should not be more than one per cent. higher than pertains to spontaneous ordinary labors. Its relative safety for the mother is unquestioned.

The mortality for the child is, and always will be, very high.

Eighteen per cent. of all babies born die within the first year. The death rate within full term for six-months time babies is nearly ninety per cent., at seven months seventy-five per cent., and at eight months fifty per cent. These figures are higher than those given by French writers, but they aim to include private as well as hospital cases. Induced labor at a period nearer term than eight months would not indicate cesarean section as an alternative operation. Efforts have been made by Prochownick and others to keep the fetal cranial bones soft up to term by diet, and so accomplish delivery without operation. The results obtained justify further effort in this direction.

The essential mortality from symphyseotomy or pubiotomy is about 2.5 per cent.; this in the hands of experienced operators and when the method was properly selected. Pinard gives five per cent. as the mortality of 160 symphyseotomies done at the Baudelocque Clinic 1892–1899, excluding seven deaths due to outside causes. The writer has operated thirteen times without a death from symphyseotomy. The general fetal mortality is given as 14.5 per cent. Pubiotomy has grown in favor of late in preference to symphyseotomy, although with equal skill and experience the operator will find no special preference.

The essential mortality from the Sänger cesarean section can be given only by estimate. Reynolds, taking the cases of Leopold, Everke, and himself in

which the patients were free from sepsis and exhaustion from labor, reports eighty-eight cases with but two deaths which occurred some years ago from operative sepsis. In the hands of operators in general we would expect a percentage mortality from selected cases of about five. For the children it should scarcely exceed the results in normal labors.

The actual mortality from the Sänger operation is from six to eight per cent. in the work of the leading operators. From all sources we find the actual mortality from cesarean section to be from twenty-five to thirty-three per cent. to-day. From symphyseotomy it is about ten per cent. The mortality from the Porro operation is necessarily higher than from the Sänger operation, even in the best of hands, inasmuch as the cause of its selection is often the septic condition of the uterus.

From craniotomy there should be in favorable cases no greater mortality than from forceps deliveries. The operation is seldom performed until after the forceps has been tried severely, and the patient been bruised and often infected. In view of the very low death rate of other methods, it should not be the primary selection of method in the hands of experienced and properly prepared obstetricians; but it may often be the most expedient method for the general practitioner, in whose hands most labors occur outside of hospitals.

Given a patient not in labor but requiring induced premature labor, symphyseotomy, pubiotomy, or cesarean section to secure delivery of a living child and an obstetrician of equal experience in each method and regularly engaged in doing abdominal surgery, due regard being given to both mother and child, in cases of medium contraction not permitting forceps delivery, symphyseotomy or pubiotomy should be selected. With more marked contraction the Bar cesarean section should be preferred. Cases of severe manipulation, with the child in good condition, with probable infection of the uterus present, call for symphyseotomy or pubiotomy in preference to the Porro operation. Symphyseotomy is not affected by infection if the writer's subcutaneous method is employed; cesarean section is markedly affected. If the child's condition renders delivery alive very problematical, further effort with forceps and then craniotomy may be best. The *a priori* argument in cases complicated by tumors and local diseases is in favor of cesarean section. Induced labor is generally decided upon by the patient.

If the physician is not accustomed to abdominal surgery, he should select symphyseotomy or pubiotomy in preference to cesarean section. If he is not accustomed to any surgical work, he should choose induced premature labor, or perform craniotomy, if he must deliver the patient himself.

The Choice of Method in Cesarean Section.—The Porro method is not only indicated but requird in all. cases of suspected existing infection of the euterus This is the situation in cases in which extensive efforts have been made by others to secure delivery by use of the forceps or by version; when the amnion has been ruptured for hours and most of the fluid drained away; when the cervix is swollen and edematous, the vagina hot and dry, and the vulva swollen; also when tumors and pathological changes are present in the soft parts which interfere with passage of the fetus; in rupture of the uterus at sites difficult to suture, or when it seems safer to do a hysterectomy than to suture a jagged wound at any site. It may be indicated in very exhausted conditions of the uterus with hemorrhage present or threatening. It is indicated in certain conditions of the very rare occurrence of combined intrauterine and extrauterine pregnancy. It is not indicated as a means of preventing future pregnancy, unless the operator is perfectly satisfied that he can perform it with the same degree of safety that he could a Sanger section.

To a physician of comparative inexperience in abdominal operations the Sanger cesarean or Bar cesarean section is probably an easier and safer method than the Porro hysterectomy.

EDWARD A. AYERS.

Cestoda.—The branch or phylum *Platyhelminthes*, commonly known as the Flat Worms, is characterized by a bilaterally symmetrical body somewhat flattened dorsoventrally and usually elongate, by the mass of parenchymatous tissue which fills all the spaces of the body, by the absence of any true body cavity, by a protonephridial excretory system, and by the complicated sexual apparatus which with rare exceptions is hermaphroditic, and which produces so-called compound eggs. Among the most prominent orders of the branch are the Trematoda (*q.v.*) or Flukes and the Cestoda or Tapeworms to be considered here.

The order Cestoda includes a large number of forms which manifest considerable differences in anatomical detail, but are comparatively uniform in general appearance and structure. The small group of Cestodaria, or Monozoa, which differ from all others in possessing but a single set of reproductive organs, and consequently but a single segment in the body, is included by some investigators in the order under consideration, but by others placed intermediate between the trematodes and the cestodes, forming as it undoubtedly does a group transitional from the one order to the other. The species of Cestodaria are, however, rare and infest the lower animals, so that they will not be discussed here.

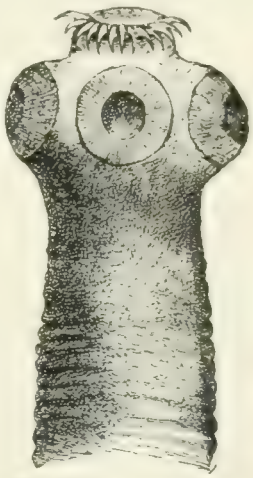


FIG. 1305.—Anterior End of *Tænia solium*, Showing Scolex, Suckers, Rostellum with Hooks, and Neck. ×45.

In the Cestoda *s. str.* the body is characteristically ribbon-like and divided into "links," segments, or proglottides. In most cases, including all the tapeworms of man, the segmentation is evident externally. At the posterior end of the chain the proglottides are larger and more distinct, and often so loosely attached as to separate from the series under the slightest disturbance. In fact such separation takes place normally as the segments become ripe. Toward the other end of the chain the proglottides grow gradually smaller and less distinct until near the anterior end it is usual to find a short region, the neck, in which no trace of segmentation is visible. The anterior end has the form of a bulbous swelling, known as the head or scolex (Fig. 1305), on which are borne the organs of fixation. The latter are either suckers, hooks, or both, and the suckers may be either elongate grooves or bothridia, cup-shaped hollows or acetabula, or, as in some marine tapeworms, of a folded form which is much more complicated.

At the apex of the head is found in the Tæniadæ a muscular organ, the rostellum which bears the hooks, usually in one or more annular rows. In form and degree of development the rostellun is a very variable organ; at the one extreme in *Tænia saginata* it is reduced to a small muscular sucking apparatus, often spoken of as the apical or fifth sucker of that species, while in other forms it is powerfully developed and capable of extension or retraction into a pocket at the apex of the scolex. It is a valuable feature in the distinction of various species.

In the head one finds the central nervous system in the form of a bilateral ganglionic mass with one or two ring-like commissures from which nerves are given off directly to the suckers and rostellum, and from which the longitudinal nerve trunks pass backward throughout the length of the chain. Three of these trunks, the main lateral nerve (Fig. 1306, *ln*) and two minor (*ln'*) are grouped together on each side of the

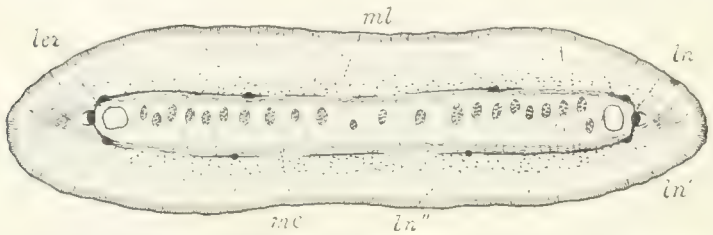


Fig. 1306.—Transection of Proglottis of *Taenia solium*, Somewhat Diagrammatic. *ln*, Main lateral nerve; *ln'*, accessory lateral nerve; *ln''*, ventral longitudinal nerve; *lex*, longitudinal excretory canal; *ml*, longitudinal body muscles: *mc*, transverse body muscles. The section is represented as having cut one of the ring commissures throughout nearly its entire extent. (Original.)

proglottis, while the two dorsal and the two ventral longitudinal nerves (*ln''*) are located nearer the median line. The various longitudinal trunks are connected by commissures which at stated intervals pass around the proglottis; they also give off branches by which the various organs are innervated.

Near the lateral nerve trunks are located the main longitudinal canals (*lex*) of the excretory system which originate in an irregular network in the head and from which are given off numerous branches often in the form of a network of fine vessels in each proglottis. In many forms a prominent transverse canal near the posterior margin of each proglottis joins the longitudinal canals (*cf.* Fig. 1307, *C*). Terminating the finer canals of this system are found the characteristic flame cells which are peculiar to this type of excretory system.

A cross-section of a proglottis (Fig. 1306) shows the various layers of which it is composed. Externally the cuticula, a resistant, elastic membrane, covers the body and is reflected a short distance inward at the various external orifices. The older view, by virtue of which an epithelium is wanting in cestodes and the outer layer represents a basement membrane, has been definitely set aside by the recent investigations of Blochmann; the cuticula is really the product of the subcuticular cells, though they are apparently separated from it by a considerable interval. Immediately beneath it occurs a delicate double layer of dermal muscles, having externally circular, and internally longitudinal fibers, the myoblasts of which lie deeper in the body. Between these fibers the bases of the subcuticular cells extend from the cuticula to the deeper lying bodies of the cells; the remaining space of the body between the various organs is filled with parenchymatous tissue. Within the parenchyma occur usually large numbers of calcareous bodies, highly refractive spherical or oval masses of small size, the function of which is yet uncertain. They are, however, characteristic features of cestode structure.

The cross-section is divided by the parenchyme or body musculature into two regions, an external cortical layer and the median area or medullary region. In the latter are found most of the reproductive organs, although in the Bothriocephalidæ the vitellaria lie in the cortical layer. The body muscles are of three sets, longitudinal, transverse, and dorsoventral or sagittal. The longitudinal muscles (Fig. 1306, *ml*) form the outer layer of the muscular mass broken only at the sexual pore, and though variable in amount are always numerous. The transverse muscles (*mc*), often called circular, constitute a plate just within the longitudinal fibers; at the side these fibers intersect and spread through the longitudinal muscles like the rays of a fan. The sagittal fibers extend singly or in small bundles from dorsal to ventral surfaces directly through the proglottid; they are scattered and not so numerous as the other systems of fibers.

Absolutely no trace of an alimentary tract has yet been discovered in the cestodes. Imbibition is the only known method of taking food, and the adult tapeworms are accordingly limited to those organs, alimentary canal and serous cavities, in which the parasite is bathed in a nutrient fluid.

The organs of the reproductive system are grouped so that each proglottis contains a complete set, and even when the body is not segmented externally, examination of the internal structure shows them to be repeated. Each proglottis contains all the organs of both sexes (Fig. 1307) and appears in this respect a complete hermaphroditic individual. The organs first make their appearance in the anterior proglottides as indistinct cords of cells which gradually assume the character of the sexually mature condition. In general the male organs reach maturity a little in advance of the female, and copulation with an older proglottis of the same or of a different chain may hence be inferred. The male system consist of numerous small testes, the vasa efferentia of which unite near the center of the segment to a common vas deferens, and the latter, which is commonly provided with an enlargement, the vesicula seminalis, and which terminates in a copulatory organ, the cirrus, opens with the vagina into a genital cloaca (*cl*) at the common genital pore, located either at the margin or on the surface of the segment. The female organs may be said to take their origin from the genital pore with the vagina

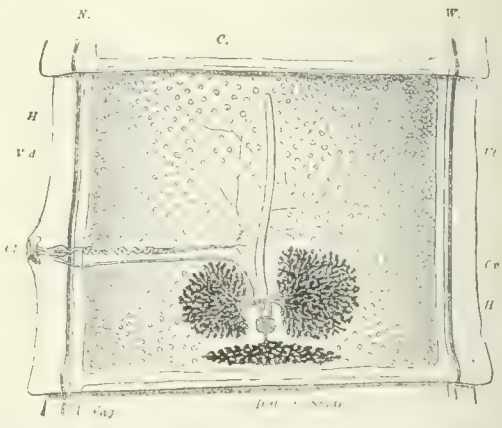


Fig. 1307.—Sexually Mature Proglottis of *Tænia saginata*. *C*, Transverse commissure of excretory canals; *Cl*, genital cloaca; *D.st.*, vitellarium; *H*, testicular follicles; *N*, lateral nerve trunk; *Ov*, ovary; *Ut*, uterus; *W*, longitudinal excretory canal. × 10.

which leads inward, furnished at some point with an enlargement, the receptaculum seminis, in which the supply of sperm is stored up. The ovary, either single or paired, empties by an oviduct which joins the vagina near the shell gland and which often has near its origin a muscular organ, the oocapt, by which the eggs are taken from the ovary and forced onward to the vagina. The vitellarium is a single, large racemose gland (*D. st.*, Fig. 1307), or a multitude of small follicles (*vit.*, Fig. 1308) in which are produced the masses of yolk material to be included in the eggs. Vitelline duct and oviduct join the continuation of the

vaginal canal in the shell gland, and to this portion of the duct the name ootype has been given. Here the ovum coming from the ovary is fertilized by the spermatazoon from the seminal receptacle, is sur-

Fig. 1308.—Central Portion of the Sexually Mature Proglottis of *Dibothriocephalus latus* from the Ventral Surface. *cir*, Cirrus sac; *or*, ovary; *o.d.*, oviduct; *sh.gl.*, shell gland; *ut.*, loop of uterus; *vag.*, vagina; *vd.*, coil of dorsal vas deferens; *vit.*, vitellaria) *vit.d.*, yolk duct. The numerous follicular testes lie beneath, *i.e.* dorsal to the vitellaria shown here. (After Sommer and Landois.

rounded by a mass of yolk material from the vitellarium, and the whole encased in a capsule formed by the secretion of the shell gland, which rapidly hardens into a thick chitinous shell. The completed eggs are then forced onward into the uterus. Since they consist not only of a fertilized ovum but also of a mass of disintegrated yolk cells, the name compound egg has been applied to them. Such eggs occur only in the flat worms.

Fig. 1309.—Ripe Proglottis of *Tænia saginata* with branched uterus. ×2. (After Braun.)

The uterus may possess a special external opening or may be without such. In the latter case it is small at first, but with the accumulation of eggs it becomes irregularly enlarged by the formation of lateral outpocketings so as to occupy with its branches almost the entire space of the proglottis (Fig. 1309). In the course of this transformation other organs gradually disappear until the ripe segment is little more than a muscular sac which encloses the branching uterus crowded with eggs. The manner of branching is characteristic of the species, as is also the way in which ripe proglottides are detached either singly or in groups, and both features together with other details in the structure of the reproductive system are discussed in connection with the individual species.

Fig. 1310.—Egg of *Tænia solium*. × 380. (After Leuckart.)

The eggs of the cestodes are oval and provided with a thin shell which is often supplied with a lid. Within this occurs in many eggs (Fig. 1310) a thicker second shell, so-called, of a structure characteristic for the family in which it occurs. In reality this inner structure is not a shell but an embryonic membrane, and takes its origin during the early growth of the germ cell, which occurs in most cases while the egg is still retained in the uterus of the adult cestode. When the uterine egg is examined soon after its formation, the shell is seen to contain a single germ cell surrounded by a number of yolk cells which, in some cases, have lost their cellular identity and constitute merely a mass of granular yolk substance.

The embryo originates from the development of the egg cell alone while the yolk cells serve as nutri-

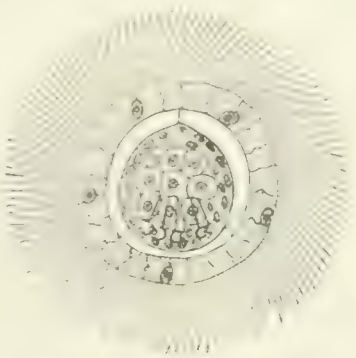


Fig. 1311.—Free Swimming Onchosphere of *Dibothriocephalus latus* with ciliated mantle. × 500. (After Schauinsland.)

ment during its early growth. From the division of the egg cell, which undergoes total cleavage, there arises a spherical embryo surrounded by one or more enbryonic membranes. From the latter may originate an inner shell, as is the case in Tæniadæ (Fig. 1310), or a ciliated mantle, as in Bothriocephalidæ (Fig. 1311). The spherical embryo (Fig. 1312), which is known as the onchosphere, is uniformly characterized by the presence of three pairs of hooks of variable shape and by great mobility, and in this condition is ready for introduction into the secondary host. This may be the result of a direct migration, as when the ciliated bothriocephalid embryo, swimming about in the water, is swallowed by a suitable host; or it may be of passive character, as when the tænioid egg containing an embryo enveloped in its membranes arrives by chance in the alimentary canal of the larval host; in the latter case, at least, it is necessary that the eggs should be introduced into the stomach and be subjected to the action of the gastric juice to disintegrate the shell and membrane. Were this not so it is clear that the harboring of the adult in the intestine would be, in those cases in which the larva parasitizes in the same animal, a source of extensive secondary infection. In such cases it is well known, as for instance in *Tænia solium* of man, that any reversal of the ordinary peristaltic action of the canal, which brings loose proglottides into the stomach and subjects them to gastric digestion, will result in the release of the six-hooked onchospheres, and in the infection of the host with the larvæ. Once that the membranes are broken down and the onchospheres set free they bore their way actively, by virtue of the hooks, through the wall, probably in most cases of the proximal portion of the intestine, and are believed to be distributed further by virtue of the portal circulation; at least the liver and the connective tissue adjacent to it are the chief seats of the larvæ. Having come to rest at such a point the embryo throws off its hooks and forms on its surface a thick cuticular layer beneath which are differentiated the muscle fibers, while about each embryo

Fig. 1312.—Free Onchosphere. Magnified.

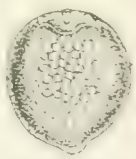


Fig. 1313.—Young Cysticercus of *Tænia saginata* with beginning of Scolex Ingrowth, Seen in Optical Section. Magnified. (After Leuckart.)

is formed a cyst by the activity of the host. The center of the sphere is filled at first with a loose parenchymatous tissue in which soon appear irregular spaces that later fuse to form a large central cavity. Thus has been reached the first form of the larval stage known as the bladder worm or cysticercus (Fig. 1313). A growth of two to four weeks is sufficient in most cases to bring the cysticercus to the diameter of a millimeter, when the second stage in the development is entered upon by the appearance of a meniscoid proliferation of cells at some point on the bladder; into this projection there penetrates from the exterior a hollow cylindrical ingrowth of the cuticula (Fig. 1314) forming the starting-point of the scolex of the

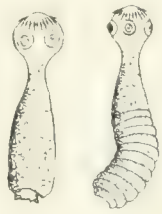
A. B.

Fig. 1314.—Formation of Scolex in Reverse on Cysticercus of *Tænia serrata*. A, Early stage; B, fully developed scolex. Magnified. (After Leuckart.)

adult worm. As the growth becomes larger the ingrowth presents the form of a flask (Fig. 1314, *A*); it is still covered throughout by a cuticular layer, and at the base of the flask there arise in reverse the structures which characterize the head of the tapeworm; at the center the rostellum with its crown of hooks, and on the sides the suckers having, when fully developed, the characteristic form and size (Fig. 1314, *B*) of the adult.

Under proper conditions the head begins to be everted, starting from the base and continuing until, with the neck, it ultimately projects above the surface of the bladder (Fig. 1315). This process may at times take place while the bladder worm is still retained within its host. In other instances the consumption of the flesh in which the cysticercus is

Fig. 1315.—Cysticercus of *Tænia serrata* with Everted Scolex (After Leuckart.)



A. B

Fig. 1316.—Young *Tænia serrata*. A, Immediately after digestion of bladder by new host; B, with a few proglottides (After Leuckart.)

enclosed and the digestion of the surrounding tissue form the stimulus for the evagination of the scolex. It is interesting to note that under the influence of the alimentary secretions of the definite host the bladder of the cysticercus is entirely digested, its remnant appearing as a ragged fringe (Fig. 1316, A), at the base of the fully extended scolex and neck. Having attached itself the scolex enters upon a period of rapid increase in length, which is soon accompanied by the appearance of the first proglottides (Fig. 1316, B). The scolex system of excretory canals originates early (Fig. 1314) even before the suckers and rostellum have appeared, and persists unchanged in the scolex of the fully developed adult.

In the formation of the proglottides it may be noted that the terminal proglottis is the oldest, and that new segments are continually formed in the vicinity of the neck. The sexual organs appear early as strings or masses of embryonic cells in the midst of the parenchyma. Formation of proglottides and growth proceed so rapidly that the tapeworm has matured and set free the posterior joints in a brief period. These reach the exterior with the fecal matter, often manifesting great independence and power in movement. They contain masses of eggs stored up in the uterus with which the beginning of the life cycle is again reached.

The normal seat of the tapeworm is in the alimentary canal, and usually in the small intestine, where the worm lies close to the wall with its head more or less embedded in the villi. Occasionally one of the smaller species wanders from this place into the ductus choledochus, and more rarely into the liver itself. This seems to be the normal habit of a few species not found in man. The occurrence of tapeworms in the human stomach or anterior thereto, as reported by various medical observers, is due either to a postmortem wandering or to regurgitation. On the other hand the reported occurrence of Cestoda in the bladder, and the discharge of proglottides from the urethra, can be explained, in so far as the cases do not rest on erroneous observations, only on the basis of injury or accidental introduction. Portions of a tapeworm have been at times discharged from abscesses or fistulæ which have probably had at some time a connection with the intestine. Leidy's discovery of a specimen in a cucumber admits, however, of no such natural explanation. Though often torpid when examined after discharge, the tapeworm is undoubtedly, it must be remembered, active in its warm-blooded host. To its contractions are due the serious symptoms which often accompany its presence. Even the discharged proglottides live for several days outside the host under ordinary circumstances and perform migrations and movements of considerable extent. By virtue of this apparent completeness and activity, the separate proglottides are frequently diagnosed as flukes.

The effect of the parasite on its host may be regarded first from the standpoint of loss of nutriment. This has been carefully computed by Leuckart for the largest human tapeworms, and amounts in one year for a single specimen of *Dibothriocephalus latus* to from 500 to 700 grams, and for *Tænia saginata* to from 1,500 to 2,000 grams. Although the presence of a number of individuals may heighten this materially, yet the amount is entirely inadequate to explain the far-reaching effects which are manifested by man as the result of the presence of only a single one of these parasites. The severe symptoms are noticeably of a nervous character. Anemia is a frequent manifestation, and this displays at times a pernicious tendency which in rare cases has terminated fatally.

Many of the symptoms affecting individuals who harbor tapeworms have been attributed to poisons developed by the parasite within the body of the host. Not only is this evinced by the subsidence of the nervous and epileptic symptoms on the removal of the tapeworms, but the affections of the eyes so frequent in those afflicted may naturally be due to the effects of a poison absorbed from the intestine and circulating in the blood. The fluid extracted from a hydatid cyst has been shown by experiment on man and animals to be toxic. To this quality may doubtless be attributed the severe symptoms or even death consequent upon the rupture of such a cyst or its operative puncture. An extract from *Dibothriocephalus latus* has been shown to exert a globulicidal effect on

dogs, and one of *Tænia saginata* has been found to kill tubercle bacilli.

The symptoms of tapeworm disease are by no means well defined and may include almost any possible combination. In experimenting upon himself, however, Stiles noted during the presence of *Tænia saginata* as the most constant symptom one not heretofore recorded. He says "During the time of infection it would very frequently happen as I walked along the street or across the room that I suddenly felt a peculiar sensation almost exactly similar to the sensation one feels upon the sudden descent of an elevator." Despite the indefiniteness of the clinical aspect of tapeworm infection, any suspicions of such trouble may be definitely tested by a microscopical investigation of the feces. The presence of adult cestodes will be manifested by an abundance of their characteristic eggs.

The specifics which are most frequently employed in driving out tapeworms are cortex granati, of which the effective principle is an alkaloid known as "pelletierine," flores kusso containing the amorphous kosotoxin, rhizoma filicis containing the amorphous filicic acid, and kamala with the resinous kamalin (see *Anthelminthics*). In bringing about the evacuation of the parasite some precautions are necessary to insure success. When a patient is passing a tapeworm the parasite sometimes breaks in two owing to the transition from the warm bowels to the cold air or to a cold porcelain vessel. By the use of a vessel containing warm water this sudden change and its consequent evil effects may be avoided. In the next place cestodes are frequently expelled in a knotted mass, and any obstruction in the lower portion of the canal may delay their passage sufficiently to permit the parasite to secure a new hold on the wall. Consequently success may depend upon thoroughly clearing out the canal.

The distribution of each species will be considered under its proper heading; here, however, some general items may be noted concerning the frequency of tapeworms. Stiles gives the following table of:

Cases of Tapeworm in Man.

Authority	Total number of cases reported.	Sex of Patients	
		Male.	Female.
Wawruck	173	56	117
Crisp	247	96	151
Seeger	26	10	16
Monti	240*	111	129
Roger	10*	3	7
Krabbe	367	126	241
Total	1,063	402	661

*Children.

He attributes the evident sex difference merely to the fact that women ordinarily prepare the food, and are hence more exposed to chance infection than men. Statistics of French maritime hospitals give for the period 1886–90 about 1.5 per cent. of cases for tapeworm infection, and records of the United States hospital service during the war contain a total of only 0.012 per cent. treated for tapeworms. This percentage is under the circumstances naturally abnormally low as compared with conditions in times of peace.

The occurrence of various species in different regions may be adjudged from the following table. Such figures exist only for a very few localities:

Authority.	Country.	Dates of records.	Total number of cases.	Tænia saginata.	Tænia solium.	Dwarf tape.	Bipal cuninum.	Hymenolepis diminuta.	Indet.
Parona	Milan	1899...	150	121	11	4			14
Parona	Italy	1868–99	513	397	71	26			19
Krabbe	Denmark	1869...	100	37	53	9	1		
Krabbe	Denmark	1869–87	200	153	24	16	8		
Krabbe	Denmark	1887–95	100	89		5	6		
Stiles	U. S. A.	1897...		Many	Rare	3		1	

Cestodes have been known from the earliest times, and both tapeworms and bladder worms are distinctly recognized in the oldest medical works which have come down to us. One of the hermetic books of the Egyptians, that on medicaments now known as the Papyros Ebers, and dated about 1550 B.C., gives in hieratic writing extensive sections on these parasites and their treatment, which are taken in part from the writings of earlier physicians. The proscription placed by Moses on the use of certain flesh has its undoubted ground in the abundant presence in such animals of bladder worms. Hippocrates notes the presence of echinococcus bladders in man and an operative method for removing them. He also speaks of the evacuation of fragments like pumpkin seeds as diagnostic of the tapeworm. Both he and Aristotle speak of the bladder worm of the pig as well known, and advise the detection of its presence by examining the lower surface of the pig's tongue where the cysticerci appear as swellings. This method is followed even to-day. Aristotle showed also that the tapeworm in contrast with the free round worms of the intestine was attached to the wall of the canal. Pliny adds to the accounts of his predecessors which he quotes only fabulous reports of the length of tapeworms (up to three hundred feet!) and erroneous observations on their presence in cold springs. Galen mentions bladder worms from the abdomen of slaughtered animals and notes the tendency of the liver to "produce" these forms in its surrounding fascia.

It was 1600 A.D., however, before even two species were differentiated among human tapeworms, and 1700 A. D. before the tapeworm head was recognized. About this time cestodes from other hosts began to be studied and the animal nature of the bladder worms, which had previously been regarded as tumors or concretions, was successfully maintained. Even then authors noted the resemblance of certain cestodes and cysticerci, and in 1782 Goeze united the two groups, but this procedure was not accepted by later authors for more than half a century.

The origin of these parasites was universally attributed to spontaneous generation, the tapeworm being said to originate from the inner wall of the canal, from surplus food of a thick character like milk or cheese, or from febrile mucous secretions, while the cysticerci were generally regarded as tumors (hydatids). This belief lasted long, even after the discovery of the eggs in many species. Linnæus was responsible for propagating another serious error, that the cestodes were free living as well as parasitic; and this was not finally refuted until the end of the eighteenth century. It was Zeder who in 1800 first divided the parasitic worms into five classes to which Rudolphi in 1804 gave the Greek names, Nematoidea, Acanthocephala, Trematoda, Cestoidea, Cystica, which they still bear. Of the last two, the tapeworms and bladder worms, Küchenmeister was able to prove about the middle of the century by feeding experiments that the latter were only developmental stages of the former, thus incorporating both in the group of cestodes. Among these those forms with only a single segment may be distinguished as the Cestodaria from the Cestoda

s. str., in which group are included the large majority of the tapeworms, and all of the forms reported from man. The latter may be arranged according to the following scheme which adopts the system proposed by Braun. The groups omitted here contain no forms recorded as human parasites. Annotation is made of the stage in which each species is a human parasite and of those forms thus far recorded in this country:

Order Cyclophyllidea		
Tænia saginata	Adult in man.	U. S. A.
Tænia solium.	Adult in man.	U. S. A.
Tænia confusa.	Adult in man.	U. S. A.
Tænia hominis	Adult in man.	
Tænia philippina.	Adult in man.	
Tænia bremneri.	Adult in man.	
Tænia africana.	Adult in man.	
Tænia marginata.	Larva in man.	U. S. A. (?)
Tænia serrata.	Larva in man.	(?)
Tænia crassicollis	Larva in man.	?
Tænia echinococcus.	Larva in man	U. S. A.
Hymenolepis nana.	Adult in man.	U. S. A.
Hymenolepsis diminuta	Adult in man.	U. S. A.
Hymenolepis lanceolata.	Adult in man.	U. S. A.
Davainea madagascariensis.	Adult in man.	
Davainea asiatica.	Adult in man	
Dipylidium caninum.	Adult in man	U. S. A.
Order Bothriocephalidea.		
Dibothriocephalus latus	Adult in man	U. S. A.
Dibothriocephalus cordatus.	Adult in man.	
Dibothriocephalus parvus.	Adult in man.	
Sparganum mansoni.	Larva in man.	
Sparganum baxteri.	Larva in man.	
Plerocercoides prolifer.	Larva in man.	U. S. A.
Diplogonoporus grandis.	Adult in man.	
Diplogonoporus brauni.	Adult in man.	
Braunia jassyensis.	Adult in man.	

The Cyclophyllidea possess a scolex with four circular suckers, often with an apical rostellum on which hooks are found when present. Segmentation is pronounced and the ripe proglottides do not separate until fully developed. There is no uterine aperture and the common sexual pore is located on the margin of the proglottides. The eggs are thin shelled and without a cover. The adults are found in the alimentary canal of the higher vertebrates.

Fig. 1317. Anterior Part of *Tænia saginata*, Somewhat Contracted. × 8. (After Leuckart.)

For the genus *Tænia* the following characteristics are diagnostic. Large species with ripe proglottides much longer than broad. Uterus with median trunk and subsequently formed lateral branches during the development of which the remaining sexual organs disappear save cirrus and vagina. Larva, a cysticercus or large bladder worm, found in herbivorous mammals and also in man; adult in man and the carnivorous mammals.

Tænia Saginata Goeze.—*T. inermis* Brera, *T. dentata* Nicholai, *T. lata* Pruner, *T. mediocanellata* Küchenmeister, *T. tropica* Moq.-Tand.*

Length 4 to 8 meters or even to 74 meters (Bérenger-Féraud). Head (Fig. 1317) somewhat four-sided, 1.5 to 2 millimeters in diameter, without rostellum and circle of hooks but with a sucker-like depression in its place which is often pigmented. Neck long, narrower than head. Proglottides number more than 1,000 and increase gradually in length until the ripe segments of characteristic pumpkin-seed appearance measure 16 to 20 millimeters long by 4 to 7 millimeters broad. Genital pores irregularly alternating, marginal, and posterior to the center of the proglottis. Uterus in ripe proglottis with median stem and twenty to thirty-five slender lateral branches, themselves often branched. Egg shell delicate with one or two polar filaments (Fig. 1318), embryophore ovoid 35 to 40μ by 20 to 30μ in diameter. Adult exclusively in small intestine of man; larva (*Cysticercus bovis*) in the muscles and viscera of cattle.

Structure.—The arrangement of the reproductive organs in a sexually mature proglottis (Fig. 1205) is best visible in a segment taken about 40 to 50 centimeters from the head. The general structure of these organs has been described above. Characteristic for this species are the two ovaries of unequal size, that at the pore side being the smaller and without the small accessory lobe cut off by the vagina as in *T. solium*. The whole proglottis has a more open aspect, and the various organs show relatively greater anteroposterior diameter than in *T. solium*. The uterus in the ripe proglottis (Fig. 1309) manifests a more crowded structure, the lateral branches are slenderer and more numerous, and two or three are stunted or lacking opposite the sexual pore.

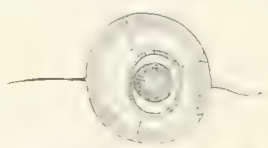


Fig. 1318. Uterine Egg of *Tænia saginata* Showing Shell with Polar Filaments and in the Center Onchosphere within the Embryophore. × 375. (After Leuckart.)

Development.—In 1861 Leuckart fed ripe proglottides of this species to calves and succeeded in obtaining the then unknown cysticercus, although various facts had pointed out cattle as the probable intermediate host. These results have been confirmed by many other investigators. At six weeks the size of the cysticercus (Fig. 1313), shelled out from its cyst, is: length 3 millimeters., breadth 5 millimeters, diameter of the head 1 millimeter; at twelve weeks corresponding measurements are 4, 4, 1.8 millimeters (length of head); at twenty-four weeks, 6, 4, 2 millimeters, at forty-eight weeks 7, 5, 2.5 millimeters. The length of life of the cysticerci is brief; at less than eight months they have been found completely calcified. A temperature of 47° to 48° C. is always fatal for them. Of course the internal portions of roasting pieces are often far from reaching this temperature. On the other hand exposure to cold-storage conditions for three weeks is sufficient to destroy all these cysticerci contained in a piece of beef.

Artificial infection of man with the adult by eating flesh containing living specimens of *Cysticercus bovis* has been tried with equal success. An average growth of 72 millimeters, or about thirteen to fourteen proglottides daily, was determined.

Anomalies.—*T. saginata* appears to be peculiarly subject to variation and malformation. Excessive pigmentation of the head and chain led to the establishment of the species *T. nigra* Laboulbène (1875) for a tapeworm expelled by a Frenchman who had lived for some time in the United States. Two genital pores, on the same or opposite margins of the proglottis, but each connected with a set of reproductive organs, indicates the probable disappearance of the segmental boundaries, and this may be manifested over a considerable stretch of the worm, giving the appearance of an unsegmented body. Welch has observed such an unsegmented region 5 centimeters in length. Intercalated proglottides or roughly triangular joints are not of infrequent occurrence. A common malformation consists in the perforation of a series of proglottides. This anomaly has received a specific name, *T. fenestrata*, at the hands of one observer. The fenestration appears first at the center of the proglottis and becomes more accentuated toward the posterior end of the chain. Its cause is probably the accumulation of eggs in the uterus with consequent

*Only the synonyms most frequently met are given under each species.

pressure on the wall of the proglottis producing a rupture when the wall happens to be thinner than usual.

Finally there occurs a prismatic or triradial variety (Fig. 1319) which was described by Bremser as the result of the fusion of two individuals. The proglottis is Y-shaped in cross section, and the scolex bears six acetabula. Specimens of this sort were named *T. capensis* by Küchenmeister and *T. lophosoma* by Cobbold.

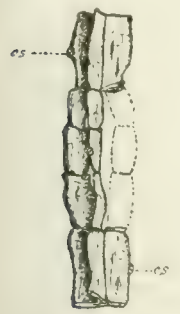


Fig. 1319.—Portion of the Chain from Prismatic Specimen of *Tænia saginata*, Showing also the Occasional Separation of the Three Wings for a Short Distance. *os*, Sexual Pore. Natural size. (After Cattaert.)

Onchospheres of *T. saginata* have been observed of considerable size, and armed with from twelve to twenty-two hooks; and Cobbold has described specimens of *Cysticercus bovis* from the heart of a calf with only three, two, one, and even no suckers on the head.

The form described by Weinland as *T. solium* var. *abietina*, from a specimen collected by Agassiz from a Chippewa Indian, is regarded by many as a small specimen of *T. saginata* with unusually dense and delicate branches of the uterus (Fig. 1320). Braun thinks it may be identical with *T. confusa* (*q.v.*). Stiles has restudied this material and regards it as a doubtful subspecies of *T. saginata*.

Distribution.—The adult occurs only in man and is cosmopolitan. Its presence in the Orient is recorded in writings of great antiquity; in Africa, Europe, and America it is also abundant, and its frequence has increased during recent years, whereas the contrary is true of *T. solium*. The evident reason lies in custom of eating beef rare, but pork well done. The figures given by Bérenger-Féraud for French maritime hospitals during the six quinquennial periods from 1861 to 1890 show a steady relative increase of cases from 0.2 to 14.8 per mille. In Paris the increase, though real, was much less, being from 0.3 to 0.6 per cent. in the same time.

The larval form, *C. bovis*, has been produced experimentally in rare instances in other hosts, sheep and goat, but many experiments on these and other hosts have been entirely without results. In its normal host (cattle) the bladder worm was apparently rare, even in regions where *T. saginata* occurred abundantly. This apparent contradiction has been explained by the demonstration that in most cases normal infection is only mild and the cysticerci are so small and scattered as not to be easily found in the beef. Their predilection recently discovered for the pterygoid muscles affords, however, a surer means of diagnosis now than was formerly known.

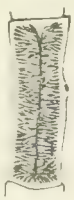


Fig. 1320.—Ripe Proglottis of *Tænia solium* (= *T. saginata* var.) var. *abietina* Weinland. (After Weinland.)

A limited number of observations on the presence of *C. bovis* in man are on record. They include cases from the brain and eye, and the determination of the species rests on the absence of hooks and rostellum. Since, however, these organs may be wanting in *C. cellulosæ*, the larva of *T. solium* (*q.v.*), the determination in the cases under discussion must be viewed with suspicion.

Pathology.—Most common in hosts between twenty and forty years of age, the beef tapeworm has been encountered in the aged and even in new-born infants. Its normal place of fixation is near the pylorus, where the head is firmly fastened to the mucosa by its suckers. It may, however, be found exceptionally in the stomach. Symptoms of its presence are direct and local in the digestive system, or nervous and reflex in character. The latter are rarer but may be severe. A. Stieda has recently described a case in which this species, in spite of its lack of hooks, had bored through the wall of the duodenum and some distance in a circuitous course into the pancreas. In this case there were neither abscesses nor preformed orifices of which the worm could have made use, while other evidence supported the view of active burrowing on its part. Possibly the rare cases in which tapeworms have made their exit through the navel or bladder may be susceptible of a similar explanation. This is, however, the only case on record which has been subjected to a thorough scientific investigation.

The proglottides of this species are expelled spontaneously and in the interval between stools. The movements after expulsion are active and long continued as is evinced by the discovery of segments high on the walls of sick-room or outhouses. The anterior margin is lacerated by separation from the chain, and in crawling the proglottis distributes eggs from the uterine branches. These detached segments are frequently diagnosed as flukes, a conclusion apparently strongly confirmed by their independent activity.

This species cannot be regarded as equally dangerous with *T. solium* since here there is no chance for autoinfection by the onchospheres. The disturbances attending its presence in the alimentary canal, however, are such as to call for its removal. Despite the absence of hooks in the species this is, as a rule, more difficult of accomplishment than in the case of the pork tapeworm. The removal of the body without the head and neck constitutes only temporary relief since the worm soon grows to full size again.

Tænia Solium L. 1767.—*T. pellucida* Goeze 1782 *T. vulgaris* Werner 1782, *T. solium* Rud. 1810. Length 2 to 3 meters, rarely 6 to 8 meters. Head (Fig. 1305) spherical 0.6–0.8 millimeter in diameter. Rostrum short, often pigmented, with a double crown of twenty-four to thirty-two hooks in which large and small alternate regularly (Fig. 1321). Large hooks 0.16 to 0.18 millimeter long, smaller 0.11 to 0.14 millimeter long. Neck long and slender. Proglottides 800 to 900 in number, at 1 meter from the head square with sexual organs fully developed; at end of chain when ripe, 10–12 millimeters long, 5–6 millimeters broad. Uterus with prominent median stem and on each side seven to ten heavy branched lateral outpocketings. Embryophores 31–36μ in diameter. Adult in small intestine of man; larva (*Cysticercus cellulosæ*) in muscles and viscera of domestic pig, rarely also of dog, man, and ape.

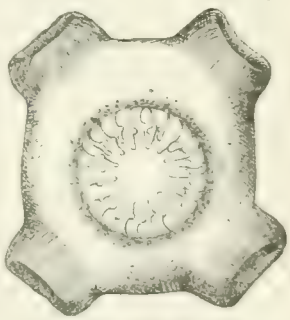


Fig. 1321.—Apical View of Scolex of *Tænia solium*. × 60. (After Leuckart.)

Structure.—In general appearance the pork tapeworm is distinctly more delicate and its chain less muscular than the beef tapeworm, previously described, and all its measurements display this difference. The scolex is decidedly smaller and has a prominent rostellum with two rows of hooks. The points of the hooks lie in a circle, but since they alternate regularly in size, the bases form two concentric circles. The hooks of the two sets show characteristic differences in figure (Fig. 1322) as well as in size.

The sexually mature proglottides do not exceed 4.5 to 5 millimeters in width by 2.5 to 3 millimeters in length, being thus decidedly inferior in size to those of *T. saginata*. On examination one sees the same organs in much the same relation as in the beef tape-

worm; but there are minor differences which serve to distinguish the two species. Most prominent is the unequal size of the two ovaries (Fig. 1323), the one next the genital pore being the smaller and being oval in outline rather than circular. In addition a small ovarian lobe lies in the angle between the vagina and the uterus, as if cut off by the former canal from the ovary to which it apparently belongs. This accessory lobe is a constant and reliable peculiarity of the pork tapeworm. One may notice also the generally compressed form of the various organs most marked in the flattened vitellarium near the posterior edge of the proglottis.

Fig. 1322.—Large and Small Hooks of *Tænia solium*. ×150. (After Leuckart.)

The differences between the two species are less evident from examination of the ripe proglottides. Usually the segments of the pork tapeworm are given off in sets of two or three rather than singly. The individual proglottis is thinner, less muscular, in general also smaller and more transparent; yet these are highly variable features and often deceptive. The form of the uterus, however, gives to the proglottis a characteristic appearance. There are only seven to ten lateral branches which are more heavily and unevenly branched, while the ends of the branches are not infrequently enlarged (Fig. 1324).

Development.—The eggs (Fig. 1310) are oval, the outer shell is thin without polar filaments and transient; the inner shell is thick, radially striated, and spherical. The onchosphere is also spherical, measuring 20μ in diameter. The development of the embryo is slow; in eight days it had only reached a size of 33 by 24μ, and at the end of three weeks its diameter was but 0.8 millimeter, while in thirty-two days different individuals measured from 1 to 6 millimeters by 0.7 to 2.5 millimeters. Even in the smallest, however, a head projection could be seen, and in the second month suckers and hooks are formed while the neck has grown so long as to produce one and a half complete circles within the bladder. By the close of the third month the bladder worm is probably ripe and capable of successful transference.

The longevity of the *Cysticercus cellulosæ* is dependent upon various circumstances. Not infrequently it degenerates at an early period, but more often later, by the loss of its liquid and by deposition of lime, into a mere calcareous granule. The same individual has, however, by means of the ophthalmoscope, been observed living in the eye for twenty years. Free cysticerci live only a brief time in water, but in flesh at normal temperature they remain living up to twenty-nine days.

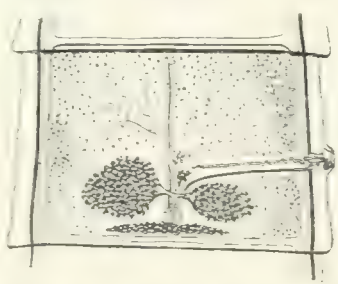


Fig. 1323.—Sexually Mature Proglottis of [illegible]. ×10. (After Leuckart.)

Many experiments have demonstrated that the *Cysticercus cellulosæ* of the pig, when introduced into the human alimentary canal, gives rise to *Tænia solium*. From ten to twelve weeks are necessary for full development and for the expulsion of the ripe proglottides. Efforts to bring the cysticercus to development in other hosts than man have as yet failed.

Anomalies.—Though less frequent than *T. saginata*, much the same malformations occur. Both incomplete and complete fusion of two or more segments and fenestration of parts of the chain are on record. An unusually slender structure of the chain gave rise to Cobbold's species, *T. tenella*, sometimes regarded as a distinct variety even yet. A scolex bearing six suckers has been observed both with an ordinary chain and with one of the prismatic or triradial variety with proglottides Y-shaped in cross-section.

Fig. 1324.—Ripe Proglottides of [illegible]. Showing Form of Uterine Branches. ×2. (After Braun.)

The onchosphere has at times more than the usual six hooks, and the *Cysticercus cellulosæ* is subject to various malformations. Absence of hooks, of a rostellum, and presence of six acetabula may be noted. Some abnormal forms have received special names; such a one is *C. racemosus* (*C. botryoides* or *C. multilocularis*) which is very irregular in form. This variety occurs especially at the base of the brain and is not surrounded by a cyst, to which, no doubt, is due its peculiar form, adapted to the space in which it lies. In some cases this variety is without a scolex or possesses at most but an abnormal rudiment of one.

Most interesting of all is the form which led to the establishment of a new species, *Cysticercus acanthotrias*, and by deduction a new tapeworm, *Tænia acanthotrias*. The *Cysticercus acanthotrias* was first observed by Weinland in 1858 at an autopsy of a white consumptive in Virginia. The bladder worms were in the dura mater, muscles, and subdermal tissues. Though in size and form like *C. cellulosæ* these hydatids (Fig. 1325) possessed three rows, each of fourteen to sixteen hooks, longer and slenderer than those of that form and measuring severally 153 to 196μ, 114 to 140μ, and 63 to 70μ. The discovery in several cases of identical bladder worms in European countries and the improbability of the existence there of an unknown large tapeworm with three circles of hooks, together with the occurrence in one case at least of this peculiar form side by side with *C. cellulosæ*, have led most investigators to regard *C. acanthotrias* as merely a variety of the common pork bladder worm.

Distribution.—*Tænia solium* is not so widely distributed as *T. saginata*, although partaking of the cosmopolitan character of the latter. It is rare in tropical lands, and wanting among such races as abstain from the use of pork. On the other hand, especially in those regions where the inhabitants are accustomed to eat the flesh of the pig in a poorly cooked condition, the parasite is most abundant. Certain provinces of continental nations come within these limits. Contrary to the statements of a number of older authorities, I am confident from the evidence gathered that this species is very rare at present in the United States. Some figures have been adduced to show that it is becoming decidedly rarer in both France and Germany. In Denmark it was, in 1869,

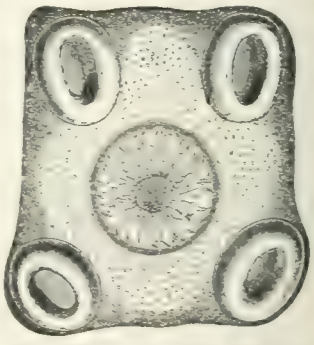


Fig. 1325.—Apical View of Scolex and Hooks of *Cysticercus acanthotrias*. ×50. (After Weinland.)

the commonest human cestode, being present in 53 out of 100 cases; in 1887–95 it was not found once in 100 cases (Krabbe).

Cysticercus cellulosæ is present not only in the pig but also in the wild boar, deer, dog, cat, rat, brown bear, ape, and even man himself. In the pig the bladder worm is more abundant in such animals as are allowed to range than in those that are stall fed. In Germany the ratio of infected animals varies in different provinces from 1 in 100 to 1 in 2,000 according to reports of meat inspectors. As these cover, however, only the cases in which the infection is prominent, the actual figures are much larger. Leuckart calculated some years ago that two to three pigs per hundred were infected. This bladder worm also seems to be growing rarer during recent years.

Pathology.—Tænia solium lies with the head fastened in the anterior portion of the small intestine. The proglottides are passed in groups with fecal matter; exceptionally through abnormal communications they reach the body cavity, bladder, and abscesses, or finally are thrown out *per os* by vomiting. The troubles caused by the worm do not differ from those due to *T. saginata*, yet the former is a much more dangerous parasite since its bladder worm may also

Fig. 1326.—Brain Cysticercus. Fresh specimen opened to show internal structure. *a-a'*, Stalk of racemose body (scolex). ×3. (After Kratter and Böhmig.)

develop in man. When abundant the bladder worms produce in pork the conditions known as "measles," and measly pork is the ordinary means of introducing *T. solium* into the human system. Rarely it may be caused by the consumption of the infected flesh of the wild pig or deer. Smoking and salting, unless extended and thorough, will not kill the bladder worms in pork and ham. Thorough cooking, however, renders them entirely harmless. As early as 1558 the cysticerci were observed in the dura mater of an epileptic. While the brain and eye are apparently the most frequent seats of the bladder worms, the latter occur also in the muscles, subdermal tissue, heart, lung, liver, peritoneum, etc. Particularly dangerous are, of course, the cerebral cysticerci (Fig. 1326) which produce effects parallel to brain tumors. In this location they are not rarely the cause of sudden death. According to Verdun and Iversenc the bladder worm of the cerebral vesicles is ordinarily free and not of the racemose variety. The acephalocystic vesicle is most common, next comes the simple form with a single head, and rarest are those consisting of a few vesicles united by the stalk. The fourth ventricle is the most frequent location of the parasite. The symptoms due to the presence of such cysticerci do not permit of certain diagnosis; most general are, however, signs of compression due to ventricular hydrocephaly.

The introduction of the onchospheres into the human stomach, which is a necessary preliminary to further development in the system, is brought about by impure drinking-water, by the use of salads or uncooked vegetables contaminated by the embryophores, and by the careless use of unsanitary closets.

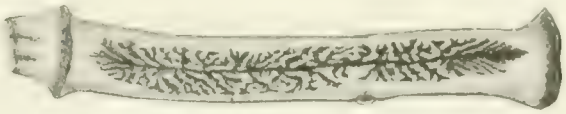


Fig. 1327.—Ripe Proglottis of *Tænia confusa*. × 2.5. (Original photomicrograph.)

More frequently, no doubt, the host of the adult tapeworm infects himself through lack of cleanliness in defecation, or possibly, as has been suggested, by internal autoinfection. Any circumstances which might lead to the passage of adult proglottides containing ripe onchospheres from the intestine back into the stomach would result in infection by those onchospheres which remained there a short time as if they had been introduced through the mouth.

The danger of internal or external autoinfection demands immediate action by the physician for the removal of the parasite under great care that all

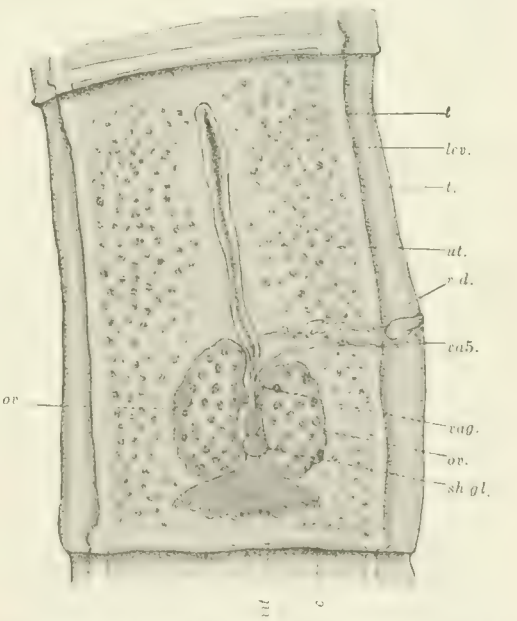


Fig. 1328.—Sexually Mature Proglottis of *Tænia confusa*. × 15. (After Guyer.)

regurgitation should be prevented. The success of the operation must be confirmed by the discovery of the tapeworm head, and the parasite destroyed rather than merely thrown away.

Tænia confusa, Ward, 1896.—This species, originally described by the writer and later studied in greater detail by one of his students (Guyer), was obtained in Lincoln, Neb. In general appearance it is much like the two species just described, but may be recognized at once by the extraordinary length of the ripe proglottides, some measuring as much as thirty-five

millimeters long by only four to five millimeters broad. The shape of these proglottides differs also from that of the terminal segments in the other species (Fig. 1327, *cf.* Fig. 1309 and Fig. 1324). The head of this species is unknown, consequently its exact position and relationship are for the time being uncertain. The whole body is tainner and more fragile than that of *T. saginata*. It measures five to eight meters in length and has some 700 to 800 proglottides, nearly all of which are longer than broad. The sexually mature proglottides (Fig. 1323) are distinguishable by the long reniform lobes of the ovary. In the ripe proglottides the median stem of the uterus bears fourteen to eighteen irregularly branching offshoots swollen at the end into irregular club-shaped masses. Of the approximately forty points of difference in structure between this and the common species, *T. saginata* and *T. solium*, as tabulated by Guyer, the most important are subjoined. Nothing is known of the life history of this species.

	T. saginata.	T. solium.	T. confusa.
Size of terminal proglottides.	12–19 mm. long by 5–6.5 mm. wide.	10–12 mm. long by 5 mm. wide	27–35 mm. long by 3.5–5 mm. wide.
Greatest breadth.	12–14 mm.....	7–8 mm.....	8–10 mm.
Length of proglottides exceeds breadth.	Only in last 100	In last half...	In nearly entire worm.
Proglottides 35 cm. behind head measure	1.5–2.6 mm long by 5–10 mm. wide.	0.8 mm. long by 1.3 mm. wide.	1–2.5 mm. long by 0.8–3 mm. wide.
Sexually mature proglottides measure.	4–6 mm. long, 8–10 mm wide.	2.5–3 mm. long 4.5–5 mm wide.	4–4.5 mm. long, 3.5–4.5 mm. wide.
Neck is.....	Unsegmented..	Unsegmented..	Segmented.
Calcareous bodies.	Abundant; to 0.018 mm.	Sparse; to 0.012 mm.	Sparse: to 0.011 mm.
Longitudinal nerve trunks.	Dorsal to genital ducts.	Ibidem . . .	Divide, passing both dorsal and ventral to ducts.
Depth of genital cloaca.	0.22 mm.....	Smaller.....	0.05–0.08 mm.
Width of genital pore	1 mm.....	Smaller.....	0.45–0.6 mm.
Ovarian lobes...	Round.....	Part of smaller cut off by vagina	Reniform.
Lateral branches of uterus.	20–30.....	7–10.....	14–18
Size and form of eggs.	0.03 mm., slightly oval.	0.03 mm., nearly round	0.039 by 0.03 mm., oval.
Pyriform process.	Present.....	In young proglottides.	Absent entirely.

Further information is needed regarding the frequence and distribution of this form, which though distinguishable on careful examination, has doubtless often been regarded as the common species—whence the name *confusa*. Braun is inclined to think that in spite of the differences this may be the same as Weinland's variety *abirtina* from a Chippewa Indian. The size of the embryophores as given by Stiles after a careful reexamination of the original material hardly conforms to this view.

A single specimen from Aschabad, Turkestan, 70 millimeters long and immature, was described by von Linstow as *Tænia hominis*. The rudimentary unarmed rostellum is 2 millimeters broad and 1.34 millimeters long with an annular ridge about its base. In the opinion of the author it cannot be the species, *Davainea asiatica*, he originally described from the same region and has the aspect of a large species like *T. saginata* or *T. solium* from which, however, it can readily be distinguished on the basis of the data given.

TÆNIA PHILIPPINA, Garrison, 1907.

Length of chain, 80 centimeters, composed of 800 proglottides, breadth 1 centimeter in maximum. Head 1 to 1.5 millimeter in diameter, suckers 0.35 by 0.40 millimeter. Neck segmented. Sexual maturity reached at about the 470th proglottis. Ovarian lobes and vitelline gland greatly elongated transversely. Uterus compact, vas deferens looped. Uterine stem spiral anteriorly and showing a V-shaped portion in posterior half of proglottis. Embryophore oval, 35 to 41μ long by 26 to 35μ broad.

A single specimen was obtained from a prison in Manila in 1905 and described by Garrison in 1907. Nothing further has been ascertained regarding its life history or distribution.

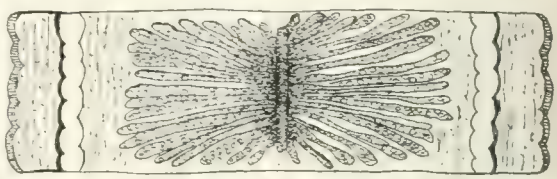


FIG. 1329.—Ripe Proglottis of *Tænia africana*. × 5. (After von Linstow.)

TÆNIA BREMNERI, Stephens, 1907.

Known only from a few proglottides passed by a native in northern Nigeria. Said to be common in that region. Noteworthy for the extreme size of the proglottides which measure in maximum 32×9 millimeters and commonly 29×10 millimeters. The uterine branches number 22 to 24; the eggs measure 34 to 45 by 30 to 42μ and average 30 by 38μ. The segments suggest strongly those of *Tænia confusa* although in the extreme the segments of the latter species are somewhat longer and narrower.

TÆNIA AFRICANA, v. Linstow, 1900.

Length about 1.5 millimeter, or more; breadth increasing posteriad, near end greatest, 12 to 15 millimeters. Scolex unarmed with apical sucker notably small, 1.4 millimeter wide by 0.5 millimeter long. Proglottides number about 600, always decidedly broader than long, ripe proglottides (Fig. 1329) measure 7 millimeters long by 12 to 15 millimeters

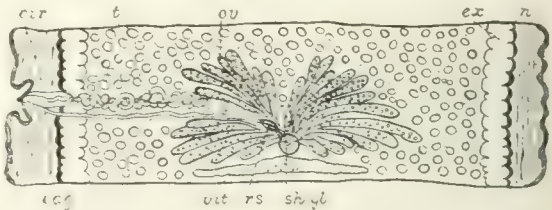


FIG. 1330.—Sexually Mature Proglottis of *Tænia africana*. *cir.*, Cirrus; *r.s.*, receptaculus seminis; *sh.gl.*, shell gland; *t*, testis; *vag.*, vagina; *vit.*, vitellarium. × 5. (After von Linstow.)

broad. Cirrus and vagina armed with minute chitinous bristles. Uterus with 15 to 24 simple branches radiating from median trunk. Eggs thick shelled, 31 to 34μ in diameter. Hooks of onchosphere 8μ long. Adult parasitic in natives, German East Africa; development unknown.

The peculiar arrangement of organs in the sexually mature proglottis (Fig. 1330) gives an easy means of diagnosing this species. The two known specimens of this form were obtained from negro soldiers near Lake Nyassa in Africa. It differs radically from the common unarmed tapeworm of man. Possibly the unknown bladder worm occurs in the zebu of which it is said that these natives are accustomed to eat the flesh raw.

Tænia marginata, Batsch, 1786.

Length 1.5 to 5 meters. Head reniform, 1 millimeter in diameter. Hooks 30 to 44 in a double row; the larger measure 180 to 220μ in length, the smaller 110 to 160μ. Ripe proglottides 10 to 14 millimeters by 4 to 7 millimeters. Uterus with short main trunk and 5 to 8 large branches on each side. Embryophores spherical 31 to 36μ in diameter.

The adult lives in the small intestine of dog and wolf; the bladder worm (*Cysticercus tenuicollis*) is found in the peritoneum of apes, cattle, sheep, and pigs. Experiment has shown that the cysticercus will not develop to the adult in the human alimentary canal. The larva has been reported twice as a human parasite; Eschricht records its presence in the liver of man in Iceland, but this is clearly an error in diagnosis. Hodges also reported its occurrence in man in the United States, but Wyman who examined the specimens stated that the hooks resembled rather those of *Cysticercus cellulosæ*, although the size of the cyst and the number of hooks favored *C. tenuicollis*. These latter features are recognized as much more variable in this species than the former, so that in all probability the determination is erroneous.

dog tapeworms are evidently most important for the physician from the sanitary point of view, quite apart from the fact that by virtue of their serious effects on other domestic animals these cestodes demand attention from an economic standpoint. A strict control should be exercised over the condition of the dog in every household where such a pet is found, and the removal of the army of stray curs should be urged in every community; for these vagrants are the very ones most likely, by virtue of their omnivorous habits, to become infected and, in consequence of their nomadic life, to carry parasites from place to place. The presence of tapeworms in dogs may be recognized by the proglottides found in the feces, and I have known of such having been taken from the back of a dog and submitted to a physician as a curiosity! Manifestation of an anal or subcaudal pruritus on the part of the dog is also good evidence of their presence. In all such cases the health of the family demands that the physician insist on the treatment of the dog for their removal.

As the determination of the species may be of importance in such cases there is appended a table, modified from Neumann, of the canines cestodes thus far reported:

- Four suckers on the head.
  - Head armed; genital pore marginal and—
    - Single
      - Numerous proglottides. Strobila several centimeters long. Segments—
        - Never more than slightly broader than long. Small hooks with guard—
          - Bifid; hooks
            - 230–260μ long, genital pore very salient. *Tænia serrata.*
            - 136–157μ long, genital pore not very salient. *T. serialis.*
          - Entire; large hooks—
            - 180–220μ long, length of mature segments double that of their width. *T. marginata.*
            - 150–170μ long, length of mature segments treble their width. *T. cœnurus.*
        - Much broader than long except the distal segments which suddenly elongate; genital pore usually large and prominent. *T. Krabbei.*
      - Three or four segments; some millimeters long. *T. echinococcus.*
    - Double and bilateral. *Dipylidium caninum.*
  - Head unarmed. Sexual orifices on the ventral surface. *Mesocestoides lineatus.*
- Two suckers on the head; genital pores on the ventral surface. *Dibothriocephalus fuscus.*

Tænia serrata, Goeze, 1782.

Length 0.7 to 2 meters. Head 1.3 millimeter in diameter with a double crown of 34 to 48 (usually 40) hooks, the larger 225 to 250μ long, the smaller 120 to 160μ. Embryophores oval, 36 to 40μ by 31 to 36μ Adult in small intestine of dog; larva (*Cysticercus pisiformis*, Fig. 1213) in peritoneum of rabbits.

Records of its presence in man from Algeria probably are based on an error in the determination. In the dog it is abundant everywhere and other cases would surely occur if the human host were susceptible. Experiments to infect man by swallowing the bladder worm have been without results.

Tænia crassicollis Rudolphi, 1810.

Length 0.15 to 0.6 meters. Head 1.7 millimeter in diameter, with a double crown of 26 to 52 hooks, the larger 380 to 420μ long, the smaller 250 to 270μ. Embryophores spherical, 31 to 37μ in diameter. Adult in small intestine of domestic cat and related wild species; larva (*Cysticercus fasciolaris*) in rats, mice, etc.

Braun records after Krabbe that in Jutland chopped mice are consumed uncooked on bread as a popular remedy for enuresis. It is apparent that the introduction of living larvæ of this species into the human alimentary canal might readily occur and the infection of man results therefrom.

Since the most dangerous of all human parasites is a dog tapeworm, and since several other canine cestodes are either known to be found or suspected to be parasitic in man at some age or in some stage of life, the

Tænia echinococcus, von Siebold, 1853.—Small cestodes (Fig. 1331) measuring from 2.5 to 5 or 6 millimeters in length with only three to four proglottides the last of which measures when ripe 2 millimeters in length by 0.6 millimeters in breadth. Head 0.3 millimeter broad with prominent rostellum bearing in a double row twenty-eight to fifty hooks which vary considerably in form and size. Onchospheres oval, 32 to 26μ by 25 to 30μ. Adult found in large numbers in small intestine of dog, wolf, jackal, dingo; the larva (*Echinococcus polymorphus*) in many organs of a multitude of hosts, including man.

Fig. 1331.—Entire Specimen of *Tænia echinococcus* from the Dog. × 12. (After Claus.)

Structure.—The adult of this species was long regarded as an immature form by virtue of its small size and limited number of proglottides until von Siebold produced it by feeding dogs with echinococcus bladders from sheep. The experiment has been repeated successfully many times with echinococcus from various sources including man, and shows a developmental period of seven to eight weeks to be necessary for the production of ripe individuals. The experimental production of the echinococcus has proved more difficult, but Leuckart has succeeded in

following it by feeding the adult tapeworms to suckling pigs. The development proceeds so slowly that in one month there has been formed a spherical solid only 0.25 to 0.35 millimeter in diameter enclosed in a connective-tissue cyst formed by the host, the entire mass making nodules in the liver barely 1 millimeter in diameter. At two months the larvæ are twice as large, the wall consists of a thick external lamellar cuticula and a delicate granular internal membrane

FIG. 1332.—Diagrammatic Representation of Echinococcus Seen in Section. *a*, Origin of a brood capsule; *b*, *c*, *d*, further stages in its development; *e*, fully developed brood capsule; *s*, endogenous daughter cyst formed from brood capsule; *g*, origin of an exogenous daughter cyst; *h*, *i*, *j*, *k*, its further development; *l*, an exogenous daughter cyst forming an exogenous and an endogenous cyst of the third generation; *m*, origin of a scolex as a minute elevation in the wall of a brood capsule; *n*, its delimitation by a shallow internal groove; *o*, later stage; *p*, the same as last, but invaginated; *q*, the enclosing of the papilla by a second outer furrow; *r*, a fully developed scolex with head inverted. (Original.)

enclosing a watery fluid. At five months the diameter of the parasite has become 10 to 12 millimeters, but no structure is yet visible in the interior. To the parasite in this condition, consisting of cuticula, parenchyma layer (endocyst), and fluid contents, the name Acephalocystis has been applied by some authors, and frequently the organism makes no advance in structure beyond this condition. Normally, however, there appears a protuberance on the endocyst (Fig. 1332, *a*) which develops rapidly into a brood capsule (*b*) in which the parenchyma is external and the cuticular layer internal. According to the views of some investigators these may become detached and continue their development floating (*f*) in the cavity of the mother cyst, in which case, however, a cuticular layer is formed on the outside and disappears within. In the opinion of others such free daughter cysts or secondary capsules arise in the wall of the parasite when a cuticular layer is formed about small centers of detached parenchyma; as these grow they burst out from the wall, and if they fall within the mother cyst and continue their development within the cavity of the latter, the form known as an endogenous echinococcus is produced; this variety occurs most frequently in man, pig, and horse. If, on the other hand, the daughter cysts burst out from the wall of the mother cyst, their continued growth (*g–l*) outside gives rise to exogenous echinococci. Evidently a group of several distinct individuals may easily be confounded with a group consisting of mother and daughter cysts. Further development may also give rise to a third generation of cysts inside the second (*l*). Any or all capsules may remain sterile, *i.e.* without heads, and such are the acephalocystic forms noted above. In most cases, however, heads are formed on the brood capsules or on the secondary cysts. According to the recent investigations of Goldschmidt a proliferation of the parenchyma layer in a brood capsule forms a low elevation (*m*). As this grows there arises inside the capsule an annular furrow, and this growing outward cuts off a pyramidal elevation (*i*) which by virtue of its early developed muscles displays great mobility, hanging outward from the brood capsule (*o*) or thrusting itself into the same as a solid unguiform structure (*p*). The external chitinous covering of the fully formed head takes its origin in a second annular furrow outside the first, which gradually surrounds the parts already described (*q*) and on its completion leaves the head projecting into the cavity of the brood capsule. Suckers and hooks originate and the entire structure presents the form of an inverted scolex (*r*). In each daughter cyst (*d*, *e*) five to ten, or even as many as thirty-four heads may develop, so that the entire number in one echinococcus reaches into the thousands. By the rupture of the brood capsule scolices may extend directly into the cavity of the hydatid or even be found floating free in its contents. The echinococcus is now mature, and if eaten by a suitable host these scolices will develop in its alimentary canal into adult tapeworms.

The form of the hydatid cyst is subject to considerable variation, the more extreme types of which have received special names. Evaginations in the wall (*s*) frequently occur under mechanical influences in the environment and suggest the origin of the form known as *E. racemosus* (Fig. 1333), from which, however, *E. multilocularis* cannot be distinctly separated in all cases. The latter, known also as an alveolar colloid, represents a mass of many small hydatids 0.1 to 5 millimeters in diameter which in section display numerous irregular cavities filled with a transparent gelatinous substance and embedded in a common stroma of connective tissue. Gall duct and boodvessels may be detected in places, but the liver cells are completely atrophied. These growths were long interpreted as colloid cancers until Virchow demonstrated their hydatid origin. The scolices or hooks, often rare and single or at most few in any bladder, are entirely wanting in forty per cent. of the specimens tested. These multilocular hydatids undergo regularly degenerative processes by which a central cavity is formed filled with a fluid containing among tissue remnants also calcareous corpuscles secondary bladders, brood capsules, scolices, hooks, hematoidin and margarin crystals, concretions, etc. The size of the hooks (Fig. 1334), which varies very considerably, is due, as Leuckart has shown, to the age and stage of development of the specimen.

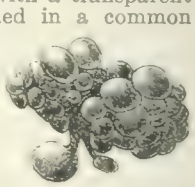


FIG. 1333.—*Echinococcus racemosus*. Natural size. (After Leuckart.)

Anomalies.—A specimen of *T. echinococcus* has been described with six suckers on the head. Regarding the larval form some observers hold that the varieties noted above as *Acephalocystis*, *E. racemosus*, and *E. multilocularis* are abnormal. According to others the latter form, which appears to be confined to Switzerland, represents a different species from the common type. Isolated cases have, however, been reported from other localities, one even from the United States (Stiles).

Distribution.—The adult parasite appears to be most common in Iceland, where it occurred in 28 per cent. of the dogs examined. In Australia the percentage is even higher, 40 to 50 per cent. being recorded. On the continent of Europe it occurs in from 0.4 to 7 per cent. of the dogs examined in different localities. Stiles records its presence, though very rarely, in dogs examined at Washington, D. C. I have found no other record of the presence of the adult tapeworm in this country. When present its occurrence in large numbers is natural. The hydatid is most abundant in Iceland and in India, where from one-fourth to three-fourths of all domestic animals are infected. In Germany, where records are of a most precise nature, the percentage of infection varies very greatly, being as low as 5 per cent. in a few cases and as high as 65 per cent. in one locality (for precise figures see Stiles and Hassall, p. 122). In the United States hydatids have been recorded from cattle, hog, and camel, and for localities in Maryland, the District of Columbia, Missouri, Nebraska, and Louisiana. In New Orleans 117 cases of liver echinococcus were recorded from 2,000 hogs.

Fig. 1334.—Echinococcus Hooks. *a*, From bladder worm of cow; *b*, from young *Tænia echinococcus*; *c*, from adult *Tænia echinococcus*; *d*, the three forms superposed to show gradual modification in form. × 500. (After Leuckart.)

In man the frequency of hydatid disease corresponds in general with that for domestic animals. In Iceland estimates of the number of inhabitants infected vary from 2 to 15 per cent.; in Australia 3,000 cases were reported between the years 1861 and 1882. In Europe the results of autopsies are given in the accompanying table, which is taken from Ostertag.

Locality.	Total number of autopsies.	Hydatids present.	
		Cases.	Percentage.
Rostock	1,025	25	2.43
Breslau	1.360	20	1.47
Berlin	4,470	33	0.76
Göttingen	639	3	0.46
Dresden	2,002	7	0.34
Vienna	1,229	3	0.24
Prague	1,287	3	0.03
Erlangen	1.812	2	0.01

In this country the hydatid is rare in man. Sommer has compiled statistics of 100 recorded cases from which the following data are taken. It is entirely unknown how many patients were infected outside the limits of this continent; certainly some of them acquired the parasite in other countries.

By Sex			
Males	17	Unstated	25
Females	28		
By Nativity.			
Azorian	1	Mulatto	2
Colored	1	Negro	2
English	5	Pole	1
Foreigners	2	Swede	1
French	2	Welsh	1
German	15	White	4
Irish	2	Unstated	54
Italian	5		
Japanese	1	Total	100
Mexican	1		
By States			
Alabama	2	New York	33
California	1	Ohio	7
Connecticut	1	Pennsylvania	10
District of Columbia	4	Tennessee	1
Illinois	3	Texas	1(+?)
Indiana	1	Vermont	1
Kentucky	2	Virginia	2
Louisiana	1 (or 2?)	Washington	1
Massachusetts	5 or 6?)	Unstated	15
Michigan	1		
Missouri	7	Total	100
New Jersey	1		

Caution should be exercised in the identification of supposed echinococcus bladders from domestic animals since the hydatid of *Tænia serialis* of the dog, which is abundant in the United States, is large, at times even of very considerable size, and produces numerous secondary bladders both internally and externally, so that the general appearance suggests that of echinococcus. The size and form of the scolices and of the hooks are so very different that even a superficial microscopic examination serves to distinguish the two forms. The hydatid of *Tænia serialis* is common in the rabbit and has also been reported from the horse.

Pathology.—The larva gives rise to the hydatid or echinococcus disease, the symptoms of which vary with the seat of the parasite. Cases are on record in which the hydatid has existed for two, four, eight, fifteen, eighteen, and even thirty years in man. It may be found in any organ, but is most frequently recorded from the liver or lungs. At times its presence is not suspected until revealed by postmortem examination; and the danger depends in any case upon the precise location and the size attained by the hydatid. In some situations hydatids exert a fatal pressure upon important vessels or nerves or destroy the tissue of essential organs. They often cause fatal results by bursting into a serous cavity or a blood-vessel, the toxic effect of the fluid having been noted already. Somer gives the following table for 1,806 cases recorded in various countries:

Classification by Habitat

	United States.	Canada.	Other countries.	Total.
Liver	62	7	942	1,011
Lung	7		140	147
Passed *per rectum*	2			2
Spleen	3	2	37	42
Brain	3			3
Abdominal wall	1			1
Vomited	2			2
Expectorated	2			2
Common bile duct	2			2
Bones	1			1
Bladder	6			6
Eye	1			1
Pericardium	1			1
Ovaries	1			1

CLASSIFICATION BY HABITAT — *Continued.*)

	United States.	Canada.	Other countries.	Total.
Uterus	3			3
Trunk and limbs			4	4
Kidneys	3		123	126
Neck (fascia)	1			1
Stomach	1	1		2
Extensors of thigh	1			1
Pleura	1		19	20
Circulatory apparatus			53	53
Cranial cavity			91	91
Spinal canal			13	13
Pelvis	3	2	70	75
Peritoneum and omentum	1		61	62
Mesentery and omentum	1			1
Female genital organs and mammaries.			60	60
Male genital organs			9	9
Face, orbit, and mouth			41	41
Neck			18	18
Abdomen	2			2
Omentum	1			1
Brain (ventricles)	1			1
Totals	113	12	1,681	1,806

Prevention.—As "hydatid disease is the most fatal zoo-parasite disease which affects man, fifty per cent. of the cases dying within five years after infection," too great insistence cannot be laid upon the necessity of guarding against the disease and stamping it out. Measures should be taken to destroy all stray dogs, to prohibit the presence of dogs at abattoirs, to destroy all hydatids found in slaughtered animals, and to discourage all intimate association with dogs. Methods for the treatment of echinococcus diseases in man have been suggested, but surgical interference alone has met with satisfactory results.

FIG. 1335.—Entire Specimen of *Hymenolepis nana* × 15. (After Leuckart.)

HYMENOLEPIS Weinland, 1858.—*Diplacanthus* Weinland.

Scolex small, rostellum retractile armed, suckers unarmed. Genital pores on left margin; three testes in each proglottis. Ripe uterus fills entire proglottis. Eggs spherical or elongated with three widely separate membranes. Larval stage a cercocystis or staphylocystis.

HYMENOLEPIS NANA R. Blanchard, 1891.—*Tænia nana* von Siebold, *T. ægyptiaca* Bilharz, *Diplacanthus nanus* Weinland (Fig. 1335).

Length 10 to 25 millimeters, rarely 40 millimeters, breadth 0.5 to 0.7 millimeters, Scolex spherical (Fig. 1336), 0.25 to 0.3 millimeters in diameter, having a retractile rostellum armed with a single circle of 24 to 30 hooks which are only 14 to 18μ long. Neck long; proglottides from 100 to 200 in number, very short, the largest measuring only 0.4 to 0.9 millimeters wide by 0.14 to 0.3 millimeters long. External egg membrane measures 30 to 40, rarely 50μ in diameter, the onchosphere membranes 16 to 20μ. Adult in the small intestine of man, and possibly also the rat.

Life History.—Grassi regards this species as identical with *H. murina* from the rat. According to him the bladder worm develops as a cyst in the intestinal villi and when full grown falls into the lumen of the canal and becomes mature. If so the chance consumption of ripe proglottides or onchospheres would ultimately produce the adult tapeworm. Moniez, Blanchard, and others have emphasized differences between the rat and the human form. In experiments with six persons who had swallowed ripe proglottides of *H. murina* Grassi obtained specimens of *H. nana* only once and this proves nothing in a region where the latter is abundant. On the other hand he was unable to infect rats by feeding them ripe proglottides of *H. nana*. The evidently close relationship of the two species is presumption in favor of a similar mode of development.

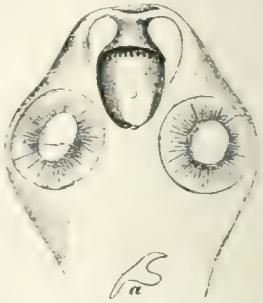


FIG. 1336.—Scolex of *Hymenolepis nana* with Rostellum Retracted. × 80. *a*, Isolated hook. × 480. (After Leuckart.)

The dwarf tapeworm which is much the smallest of all human cestodes and accordingly difficult to detect was formerly regarded as very rare. Now it is known to be exceedingly common. Discovered in 1851 by Bilharz in Egypt in enormous numbers at an autopsy, it has since been reported from nearly every part of continental Europe, from Siam, Japan, and the Philippines, and may justly be regarded as cosmopolitan in its distribution.

To the single record in the United States of Spooner in 1873 reported in the previous edition of this work, have been added about 200, most of very recent date, observed since attention has been directed to the parasite. Ramsom (1904) published a valuable monographic account of the worm and its effects with 116 cases. These and later cases show that the parasite is generally distributed over the Southern States, and occurs also in New York, Philadelphia, and Colorado. Doubtless future study will result in extending its range still further. The cases occur in general under unfavorable hygienic conditions and infection is probably traceable to the contamination of food by mice and rats. Uncleanly habits will no doubt result in autoinfection, but the eggs produced in the intestine of the host and discharged *per anum* must be introduced *per os* and undergo stomach digestion before they will hatch. These conditions explain the greater frequence of the parasite in children and especially in infants. The parasite rarely occurs in adults. When present it is often found in large numbers, even up to 4,000 or 5,000 in a single host.

The infection is diagnosed by the discovery of the cestode or more commonly its eggs in stools. The difficulties in diagnosis have been shown by Bass and Gage who adopt centrifuging to secure the eggs which are easily recognized when found. In some cases gastric disturbances and reflex nervous symptoms are present; these may become severe and may rise to obscure gastrointestinal or nervous disorders in children (Schloss) or adults (Bass and Gage). Male fern is said by some to be the only remedy of value and to expel the worms readily; but others find repeated treatment necessary even with this drug, and still others report thymol efficacious. I have myself discovered specimens among hook worms removed in Kentucky by thymol treatment; the cestode was neither suspected nor recognized.

HYMENOLEPIS DIMINUTA R. Blanchard, 1891.—*T. diminuta* Rud., *T. leptocephala* Creplin, *T. flavopunctata* Weinland, *T varesina* Parona, *T. minima* Grassi.

Length 20 to 60 centimeters, width 3.5 millimeters. Head small, claviform, with rudimentary unarmed rostellum; neck short (Fig. 1337). Proglottides short and indistinct at first, increasing gradually to a maximum near the posterior end of the chain of 0.66 millimeters long by 3.5 millimeters wide. External egg membrane 60 to 86μ in length, internal with polar projections; onchosphere 36 by 28μ. Adults in the small intestine of various rats and mice, and rarely also of man; larva (cercocystis) in various insects, chiefly the meal worm (*Asopia farinalis*).

Fig. 1337.—Anterior End of *Hymenolepis diminuta*. Magnified. (After Zschokke.)

This typical species has been studied with great care by Zschokke. The structure of the sexually mature proglottid is shown in the figure (Fig. 1338). In the ripe proglottis the egg-filled uterus occupies the entire space within the walls of the segment save for the large flask-shaped cirrus. Sterile proglottides of smaller size and without eggs occur at times in the series.

The larval form, a cercocystis, occurs usually in the larva and adult of the meal moth (*Asopia*).

It is recorded also from the earwig (*Anisolabris*) two beetles (*Akis* and *Scaurus*) and by Nickerson at Minneapolis also in two thousand-legged worms (*Julus* and *Fontaria virginia*). The adult has been developed in white rats and in man. In the latter fifteen days after feeding the larvæ ripe eggs were found in the feces.

Fig. 1338.—Reproductive Organs of *Hymenolepis diminuta*. (Letters as before.) Magnified. (After Zschokke.)

Nearly a score of cases are recorded; the first specimens were taken in Boston by Palmer in 1842 and described by Weinland in 1858. Leidy recorded it from Philadelphia in 1884; Packard from the same place in 1900; Deaderick from Arkansas in 1906, and Nickerson from Minnesota in 1911. The other cases are from Italy, France, and South America. As its normal host, the rat, is cosmopolitan, and as its larval hosts occur in and about food, its occasional appearance as a human parasite is to be expected. Infection is undoubtedly caused by the consumption of food containing infected insects.

All cases except one concern children or infants, and only mild infections and corresponding symptoms are recorded. The worm is readily diagnosed by its ova in the feces of the host and any anthelmintic will expel the parasite. Even a cathartic has brought it away and in one case it was expelled without medicine.

Fig. 1339.—Anterior End of *Davainea madagascariensis*. ×14. (After Blanchard.)

A third species, *Hymenolepis lanceolata* has also been reported from the human host in Europe. It is a normal parasite of geese, ducks, and other water birds and the larva is said to occur in small water animals (Copepoda). Human infection undoubtedly is caused by drinking water containing such animals infested with the larval cestode.

Davainea. R. Blanchard, 1899.

Scolex spherical with prominent rostellum sometimes retractile, armed with many small hooks in two rows which may be caducous. Genital groove unilateral or alternating irregularly. Eggs grouped in capsules. Development unknown.

Davainea madagascarensis R. Blanchard, 1891.—*Tænia demerariensis* C. W. Daniels, 1896.

Length 25 to 40 centimeters with 500 to 600 proglottides. Head (Fig. 1339) includes retractile rostellum having many hooks, 23–25μ in length, which are usually partly lacking. Genital pores unilateral with occasional transpositions. Ripe proglottides 2 millimeters long, 1.4 millimeters broad. Eggs in groups of two or three with heavy capsules of parenchyma forming the characteristic egg balls 0.2 to 0.4 millimeters in diameter which fill the entire ripe progottid. Onchosphere 8μ, or 15μ (Garrison), in diameter with 6 delicate nearly straight hooks 4 to 5μ long.

The growth of the cestode is very rapid. At 3 centimeters from the head proglottides may be seen in copula. The last hundred segments, which make more than half of the entire length of the worm, contain only eggs about which the capsules are forming (Fig. 1340). Of the development nothing is known.

The ten cases reported are widely distributed, coming from Madagascar, the Antilles, Siam, British Guiana, and the Philippines, and show its general occurrence throughout the tropical belt. The first six cases were all from young children, and the last two from adults. All cases have been found in seaport towns and have been apparently related also to ships and docks. Blanchard surmises that these facts pointed to some cosmopolitan insect found in such localities as the intermediate host and suggests the cockroach. But the investigation of tropical regions has hardly begun and the parasite may be even more frequent in the interior of these countries. Many have accepted the view that this tapeworm is an occasional or erratic parasite of man and its normal host is some other animal. Blanchard and Garrison question this explanation since the species have never been reported from any other host; but its infrequence in man and the lack of knowledge concerning the regions where it occurs are strong arguments on the other side of the question

Fig. 1340.—Ripe Proglottis of *Davainea madagascarensis* just Liberated from the Chain. × 10. (After Davaine.)

Of special interest to American physicians is the recent report of Garrison (1911) that this species occurs in Manila. The specimens were obtained at the necropsy of an adult male Filipino. The case is the first from that part of the world and one of two only from adults. The detection of its presence under such circumstances may indicate a wider in-

fection of the human host than heretofore assumed. A parasite of such insignificant size would probably be unnoted unless present in large numbers or in young children where the disturbance to normal functions would be relatively greater.

Davainea asiatica (v. Linstow) 1901 was described from a specimen in the St. Petersburg museum. This came from Asia, near the Persian boundary, east of the Caspian Sea. It is imperfectly known but apparently cannot be identical with the previous species.

FIG. 1341.—Anterior End of *Dipylidium caninum*. (Original.)

DIPYLIDIUM R. Leuckart, 1863. Rostellum retractile, armed with several annular rows of alternating hooks. Genital pores opposite, sexual organs doubled. Uterus a reticulum which later becomes changed into sacs holding one or more eggs each. Eggs with double shell.

DIPYLIDIUM CANINUM Railliet, 1893.—*T. moniliformis* Pallas, *T. cucumerina* Bloch, *T. elliptica* Batsch.

Length 15 to 35 centimeters; maximum width 1.5 to 3 millimeters. Scolex (Fig. 1341) small, rhomboidal with retractile club-shaped rostellum armed with 3, or 4 rows of thorn-shaped hooks, decreasing in size from 15μ in the first row to 6μ in the last. Suckers elliptical, neck very short. First proglottides small, becoming trapezoidal and finally characteristically of melon-seed form. Genital pores symmetrical on both sides. Egg sacs contain 8 to 15 eggs; the ripe proglottides have a distinct rose tint. Eggs spherical, 43 to 50μ in diameter. Onchospheres 32 to 36μ in diameter. Adult an abundant parasite in the small intestine of the dog, and cat; rarely also in man; larva (cryptocystis) in the body cavity of the dog flea and dog louse. In this species the doubling of the reproductive organs is striking, a complete set with genital pores and copulatory organs being present on each side of the proglottid (Fig. 1342). The branches of the uterus, however, become cut off as small capsules containig 8 to 12 eggs each; and in the ripe proglottid the mass of such capsules fills the entire middle field, and a reddish-brown substance deposited about the eggs imparts the characteristic pink color to these segments. Prismatic and doubly fenestrated specimens have been observed and also individuals in which four sets of organs lay in a single proglottid.

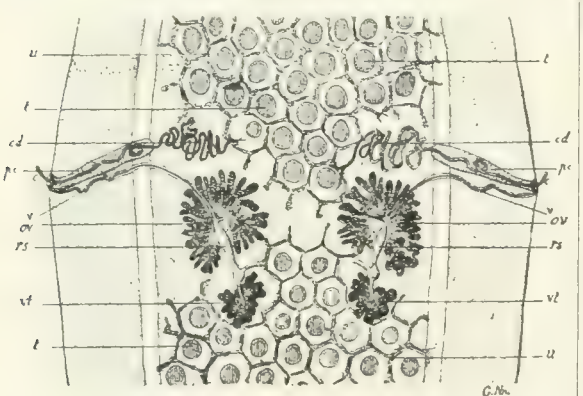


FIG. 1342.—Median Portion of Sexually Mature Proglottis of *Dipylidium caninum*; *c*, cirrus; *ov*, ovary; *rs*, seminal receptacle; *t*, testis; *u*, uterus; *v*, vagina; *vt*, vitellarium. × 25. (From Railliet, after Neumann.)

The onchosphere is transformed in the body cavity of the dog louse, dog flea, or even of the human flea, into a tailed larva or cryptocystis. When the dogs, annoyed by the work of the fleas, hunt and destroy these pests it is easy to see how they infect themselves.

While formerly this species was regarded as very rare, within recent years cases of its occurrence have been recorded with increasing frequency until now at least 75 to 100 cases are known. The first on record dates from Linnaeus. Only two cases have been reported in this country, by Stiles and by Riley, but doubtless it is not uncommon among children. From 75 to 85 per cent. of recorded cases concern children under three years of age. Infection comes from accidental ingestion of dog fleas that harbor the bladder worm stage, and intimate association with pet cats and dogs favors such transmission. Younger children pay less particular attention to the condition of food and drink with resulting increased liability to infection. The relatively large number of cases reported from Germany is explicable on the basis of more careful microscopical diagnosis in German medical practice as the parasite and the opportunities for infection are abundant everywhere. In various parts of the United States the tapeworm occurs in numbers, especially in the smaller dogs and in cats.

The order of the Bothriocephaloidea is characterized by the presence on the scolex of two poorly developed sucking grooves which occupy the dorsal and ventral surfaces and in some cases are modified in structure. Of the three sexual pores the uterine aperture lies always on one surface of the proglottis whereas the two others may be on the same or opposite surface, or on the margin of the proglottis. The sexual organs are generally single, rarely doubled; this development does not transcend the stage of maturity so that no parts degenerate. Eggs usually with cover; much like trematode eggs. Of the many forms known only a few are of immediate importance here.

DIBOTHRIOCEPHALUS Lühe.

Scolex elongated, suckers unarmed, not powerfully developed. Genital organs single. Genital pores in midventral line. Uterus in coils in center of the proglottis producing a characteristic rosette figure (Fig. 1343). Eggs brown, thick-shelled with cap.

DIBOTHRIOCEPHALUS LATUS Lühe, 1899.—*Bothriocephalus latus* Bremser, 1819; *Tænia vulgaris* and *T. lata* Linnaeus, 1748; *Dibothrium latum* Diesing, 1850.

Length 2 to 9 meters, rarely up to 20 meters. Grayish yellow. Head oval, or almond-shaped, 2 to 3 millimeters long, 0.7 to 1 millimeter broad, traversed longitudinally by two lateral grooves. Proglottides 3,000 to 4,200 in number, usually broader than long but becoming gradually quadratic. Sexual pores on midventral line, cirrus and vagina opening close together and in front of uterine pore. Eggs 68 to 70μ by 45μ. Adult parasite in small intestine of man and cat; larva (plerocercoid) in the muscles and among the viscera of many fresh water fish.

Structure.—The longitudinal sucking grooves, characteristic of these forms, occupy in reality the upper and lower face of the head, appearing at the sides in consequence of the torsion of the neck. This species can be distinguished easily from the other large human cestodes, *Tænia saginata* and *T. solium*, by the thickened area in the center of the chain and by the dark irregular rosette figure in this area. The arrangement of the sexual organs in the proglottid (Fig. 1308) also differs radically from that in the genus *Tænia*. The numerous tests occupy a dorsal position on both sides of the segment and vas deferens extends in loops toward the anterior end, terminating in a muscular cirrus pouch with a seminal vesicle. Next the male genital pore lies the orifice of the vagina

which passes directly posteriad in the median line and after forming a receptaculum seminis joins the common yolk duct near the center of the voluminous shell gland. The vitellaria or yolk glands are racemose structures occupying the cortical layer of the segment in the lateral fields; their numerous ducts converge and ultimately unite into the common yolk duct noted above. The paired ovaries lie one on either side of the shell gland in the posterior region of the proglottis and the oviduct joines the vagina and yolk duct in the shell gland. From the union of these ducts originates a canal which expands and as

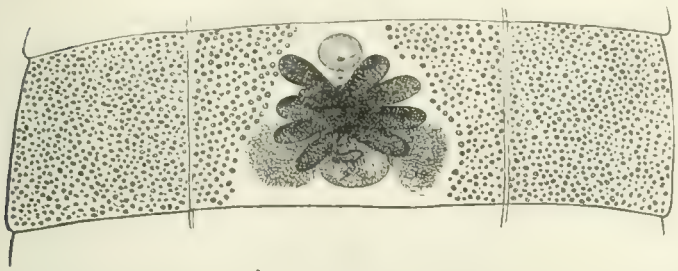


Fig. 1343.—Ventral Aspect of Sexually Mature Proglottis of *Dibothriocephalus latus*, Showing Female Reproductive Organs. (*Cf.* Fig. 1308.) × 12. (After Leuckart.)

the uterus lying in irregular loops ventral to the vas deferens extends forward to the special uterine orifice, a simple pore in the midventral line a short distance behind the common opening of cirrus and vagina. In the last proglottides the uterus is often empty of eggs and the genital glands are atrophied.

Development.—Ripe proglottids contain numbers of brownish, elliptical eggs in which may be distinguished the egg cell surrounded by masses of yolk cells. These eggs are discharged abundantly in the feces of the host. After lying in water several weeks a ciliated onchosphere (Fig. 1311) is hatched out and swims slowly about in the surrounding water. Sometimes this larva throws off the ciliary covering, sinks to the bottom and creeps about. If left alone it dies ultimately without attaining any further development. The bladder-worm of *Dibothriocephalus latus* was first discovered by Braun in the muscles and viscera of food fish in the Baltic provinces. It is an elongated form known as a plerocercoid (Fig. 1344), and measures 8 to 30 millimeters in length. These larvæ were abundant in fresh fish from Dorpat markets, and living specimens were also obtained from smoked, salted, and frozen fish as well as in roes of the pike which salted are eaten raw as caviar. About a dozen kinds of fresh water fish may be infected. Experimentation on dogs, cats, and man established the connection of this larva with the adult *Bothriocephalus latus*. Other authors, notably Zschokke in Switzerland (Geneva), have discovered the larva in perch, salmon, trout, grayling, and whitefish, and in some instances have determined experimentally their relation to the species under consideration, confirming fully the discoveries of Braun. In Scandinavia, Lombardy, Switzerland, and Japan the existence of the plerocercoid in various fishes and the consumption of some of the latter in a raw condition by the native population explain the method of human infection which has been further demonstrated experimentally in specific cases.

Fig. 1344.—Plerocercoids of *Dibothriocephalus latus* from Pike. *A*, Natural size; *B*, *C*, with scolex protruded and retracted × 2. (After Leuckart.)

Once introduced into the human alimentary canal the development of this tapeworm is very rapid; the growth reaches 6 to 9 centimeters per day in the various cases. Eggs appear in the feces of man in from twenty-four to thirty days after infection.

Anomalies.—Slender specimens (var. *tenella*) have been recorded as also some with exceptionally larger proglottids. One specimen of the prismatic variety is on record (cf. *T. saginata*) and double fenestration is not rare. Most frequent however is the reduplication of the genital pores and organs which Leukart says he has never failed to find in some proglottid of each specimen examined.

Under a separate name (*B. cristatus*) Davaine described a variety which is distinguished from the common form by possessing a projecting longitudinal ridge on each flat surface of the head

Geographical Distribution.—This mode of infection from fish explains the occurrence of this parasite which in certain regions is extremely abundant and in others equally rare. Around the shores of the Baltic it is common, especially in Russia and East Prussia; in Finland and Sweden it is hardly less abundant, but in Germany, Holland, and Belgium it is occasional. Endemic centers are found like that in Munich and around Lake Stannberg in Bavaria. In Roumania it seems to be general and in the district about Lake Geneva, Switzerland, it has been very common; according to Zschokke it is growing rarer in the city of Geneva, as its frequence has fallen in thirty years from ten per cent. to one per cent. During the eighteenth century it was abundant in Paris but now occurs only in cases introduced from without.

In Japan and Turkestan the broad tapeworm is said to be the most abundant parasite of man and to occur generally in dogs and cats. In Africa a center is reported to exist around Lake N'gami, and the parasite is also recorded from Angola and from Madagascar. In these cases the record may apply to some allied species, one of which at least has been described from the African continent. This or some related species may confidently be expected when regions little known and dependent on fresh-water fish, such as those near the Arctic and North Pacific, or Bering Sea, are investigated.

In this country the broad tapeworm was formerly regarded as a rare curiosity; in recent years it has been reported many times. About one hundred cases are listed of which sixty-five are recorded from Minnesota by Nickerson. The first case was studied by Leidy in 1879. Like many of the later cases it was observed in Philadelphia and was imported as the host, a Swede, had been in this country only a few months. The large majority of American cases concern Russians and Scandinavians some of whom, however, had been here for several years. In many it is reported that the patient had been entirely free from symptoms. Willson (1902) published a most careful study of cases involving anemia and included data on earlier American records. In 1906 Nickerson reported cases in Finns living in Minnesota, and one of them was a child that had never been out of the state. A series of similar cases of later date from Nickerson and Warthin has confirmed this view that there exist centers of infection in this country. The bladder worm has not yet been found in American fresh-water fish, although I know that plerocercoids indistinguishable from that of *Dibothriocephalus latus* occur in fish from the Great Lakes and from smaller inland lakes near them. No evidence has yet been adduced to show whether the species is autochthonous or whether it was introduced by immigrants who thereby infected native species of fish in waters adjacent to their places of residence. There can be little doubt that northern waters are infected and

especial care must be taken to avoid the consumption of imperfectly cooked fish since this species ranks rightly as one of the most serious of human parasites. The infection can be spread through dogs and cats which are hosts of this species and thus the original area of infection is likely to be extended widely. The infected areas known at present are located in North Dakota, Minnesota, and northern Michigan. In the absence of well-enforced protective measures these centers are likely to repeat the experience of communities in the Old World and become generally and heavily infected. There is absolutely no danger of direct infection from carriers of the adult tapeworm and the factors to be guarded are infection of fish by sewage contaminated with eggs, and consumption of insufficient cooked fish.

Pathology.—The parasite is sometimes solitary, though several individuals occur together in the majority of cases and nearly one hundred have been recorded from a single host. Evidently its frequence depends upon the habits of the individual in eating raw or poorly cooked fish, no less than upon the locality. The effect of the parasite is often unnoticed; in other cases are noted gastric and nervous disturbances, and in some instances an extreme anemia.

This so-called bothriocephalus anemia is characteristic of certain cases of infection with this parasite. The symptom complex is typical of progressive pernicious anemia which according to Huber gives the disease a mortality of sixteen per cent., for unless the worm is removed the case terminates fatally. In some cases this occurs even though the parasite is discharged as the system seems unable to react from its depressed condition. It has often been noted that in certain individuals several parasites produce no effect and yet in others a single worm causes a profound anemia. The method of cure is the prompt expulsion of the parasite. Within a few hours after this the condition of the patient undergoes marked improvement and most cases recover absolutely. If the removal of the worm is only incompletely effected the symptoms will return when ripe segments are again ready to be discharged. This species is most difficult to expel completely and in consequence recurrence is frequent. Thymol is highly recommended and pelletierine preceded by twenty-four hours starvation and followed by a purge has yielded most successful results. An enema is useful in aiding in the evacuation of the worm when free. Return of the difficulty may be expected when the head is not secured although it is often destroyed and not found.

The cause of the anemia is generally regarded as a toxin which brings on increased albumin disintegration. The removal of the worm is followed in most cases immediately by well-marked nitrogen retention. Tallquist extracted from ripe segments of *Bibothriocephalus latus* three well-differentiated substances: a proteolytic ferment (Bothriocephaloenzyme), a hemagglutinin (Bothriocephaloagglutinin), and a hemolysin (Bothiocephalolysin). Later he ascertained that the hemolytic lipoid substance was oleic acid mostly combined with cholesterin. The anemia was accompanied by increased absorption of oleic acid due to a local stimulant which could be extracted by ether from proglottids of the worm.

According to his investigations the hemolytic substance is not eliminated from the cestode during life, but only as the terminal proglottids go to pieces or the entire chain is destroyed by some unfavorable condition. Then this substance is set free and absorbed by the host with the result of producing an anemia. This view is supported by clinical observations; in 70 per cent. of Schauman's cases with anemia the parasite was disintegrating or had gone to pieces.

DIBOTHRIOCEPHALUS CORDATUS R. Leuckart, 1863.—*Bothriocephalus cordatus* Leuckart.

Length 80 to 115 centimeters. Head 2 millimeters in diameter flattened, cordiform, with deep sucking grooves on ventral and dorsal surfaces. No neck. Segmentation begins directly behind the head (Fig. 1345); the proglottides which increase rapidly in width become mature within 3 centimeters, the largest proglottides measure 7 to 8 millimeters in length by 3 to 4 millimeters in breadth and number about 600. Eggs, with cover measure 75μ by 50μ. Adult parasitic in seal, walrus, dog, and man in Greenland; larva unknown, undoubtedly in some fish.

In Greenland and Iceland the adult is a common parasite in various hosts, but records of its presence outside of Greenland are based on errors. The supposed introduction of the species into Germany with Eskimo dogs rests upon an incorrect determination of the form observed. At most sporadic cases might be met in natives from those regions where it occurs, on its visitors to them.

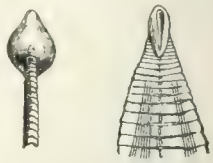


FIG 1345.—Anterior End of *Dibothriocephalus cordatus* in Lateral and Surface Views. ×5. (After Leuckart.)

Dibothriocephalus parvus Stephens, 1907, is reported from Tasmania. As the host was a recent immigrant from Syria, the parasite may have been imported from the Levant and not be of Australian origin. The form is readily distinguished from both the preceding species by marked smaller size of body and of eggs, and by absence of calcareous corpuscles.

SPARGANUM MANSONI Stiles and Taylor, 1902.—*Ligula mansoni* Cobbold; *B. liguloides* Leuckart, *Bothriocephalus mansoni* R. Blanchard.

Adult unknown; larva a pleroceroid. Length 12 to 60 centimeters; breadth 3–6–12 millimeters flattened, without proglottides but markedly irregular folds. Anterior end enlarged, bearing the head which may be drawn in or evaginated and on which two faint bothria are visible. Pararasitic in connective tissue of man in Japan and China.

Twenty cases of the occurrence of this parasite are reported, a few from Amoy and the majority from Japan. It was first found by Manson in an autopsy when from one host a dozen specimens were taken from below the peritoneum and one found free in the peritoneal cavity. Ijima and Murata have described in detail seven cases from Japan; in three the parasite was passed with urine or taken from the urethra, in three also it was drawn from tumors on the eye, and in one from a cavity in the subcutaneous connective tissue of the thigh. Miyake has added recently other cases from Japan.

Apparently the larva wanders about in the body of its host in which, as in several cases described, it may remain active for some time, even as long as nine years. Ultimately it reaches the surface of the body or of an internal organ (bladder) from which it eventually attains the exterior.

The occurrence of such a larval form in man is accidental and yet indirect evidence points to the frequence of this occurrence in some parts of the East. What is diagnosed as the same species is reported from an ape and a marten in the East and from the jackal in Egypt. Since these parasites are larvæ with no trace of reproductive organs confusion in diagnosis is easily possible and the reports may concern several species. Of the origin and further development of all of them nothing is known. The geographical distribution of the human forms, the unusual size of the specimens, and the presence of two longitudinal furrows on one surface of the body, are suggestive that this form may be the larva of *Diplogonoporus grandis* (*q.v.*) of which the adult alone has been described.

Another such larval species, *Sparganum baxteri*, has been described from British East Africa; and the list of similar occurrences is likely to be still further extended in time. There is no reason for considering them other than occassional parasites of man.

PLEROCERCOIDES PROLIFER Ijima, 1905.—*Plerocercus prolifer* Ijima; *Sparganum proliferum* Stiles, 1906.

Larval form; adult unknown. Length 1 to 12 millimeters, breadth about 2.5 millimeters. Head more motile than rest of body; without bothria, with rudimentary apical sucker. Capable of reproducing by transverse division and of budding off extra scolices (Fig. 1346) which may separate to form new individuals. Life history unknown. Found encysted in subdermal connective tissue in man. Two cases on record from Japan and Florida.

The first case, reported by Ijima, concerned a Japanese woman of lower class who harbored enormous numbers of this parasite. She came to the hospital for the treatment of an inguinal hernia, treaceable to the presence of these parasites in Poupart's ligament. The integument of the thigh was swollen and

FIG. 1346.—Budding Scolias of *Plerocercoides prolifer*, larval form. Magnified. (After Ijima.)

bore scattered spots of acne-like character. The dermal affection which had much the appearance of elephantiasis had been noticed for two years. Itching led to scratching and consequent breaking of the skin from which came out soft whitish masses with fluid. Superfluous tissue removed to relieve the patient showed that the subcutaneous tissue was several centimeters thick and rich in lymph. Numerous capsules containing worms were visible in all parts of the tissue.

These capsules were spherical or ovoid and measured 1 to 3 millimeters in diameter by 2 to 8 millimeters long. They consisted of a dense felted layer of connective-tissue fibers formed by the host. The number was estimated to be considerably over ten thousand in the left thigh alone. Some parasites were without any capsule and such were extended, slender and simple. When liberated from the capsule and placed in warm salt solution the worms manifest some motion, most evident at the head which was retracted and again everted. In the course of such movements a small apical depression appeared and vanished. The body showed at most slow vermiform movements.

The larger capsules contained several worms and the shape of many specimens shows that this form has the power of dividing transversely and of budding to produce new individuals, thus increasing the infection of its host. The buds thus formed are motile when the parent stock shows no motion. From this method of growth result shapeless masses (Fig. 1347) in which the original head is indistinguishable. The enormous infection of the host is undoubtedly traceable to the ability of the larvæ to multiply asexually. The structure of the larva shows it to belong to the Dibothriocephalidæ. Experimental infection of pigs and dogs and cats was tried without success.

Two years later Stiles described a similar case from Florida. The trouble was of much longer duration, having been first noticed apparently twenty-five years before. The infection increased with time from a few pimples to many which enclosed larvæ similar to those of the Japanese case. Another case is believed to have existed earlier in the same region.

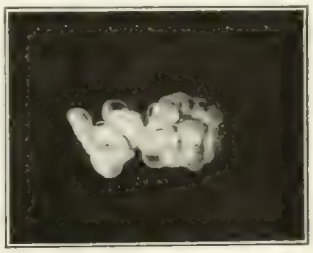


FIG. 1347.—Mass Resulting from the Budding of the larva of *Plerocercoides prolifer*. (After Ijima.)

The only difference observed between the larvæ from Florida and Japan was the size of the calcareous corpuscles. The widely separated localities agree in proximity to the ocean and fish formed a considerable part of the diet of both patients. The parasite is unquestionably a serious menace by virtue of its power to multiply in the host and it is of great importance to determine the origin of the parasite in order to guard effectively against its introduction into the human host.

DIPLOGONOPORUS Lönnberg, 1892.—*Krabbea* R. Blanchard, 1894.

Scolex with powerfully developed sucking grooves. No neck. Genital organs double in each proglottid, but each group is identical with those of *Dibothriocephalus*. Genital orifices of each set ventral on either side of median line of body forming a series which corresponds to the median line of the uterine fields on that side of the chain.

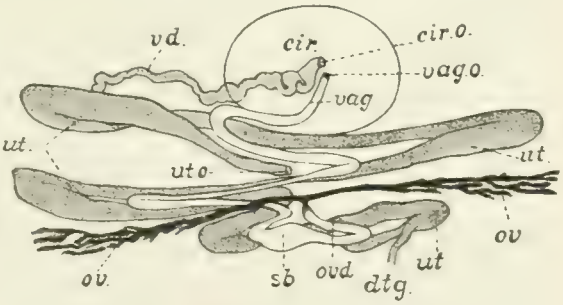


FIG. 1348.—Sinistral Set of Reproductive Organs from Sexually Mature Proglottis of *Diplogonoporus grandis*. × 140. (After Iijima and Kurimoto.)

DIPLOGONOPORUS GRANDIS, Lühe, 1899.—*Krabbea grandis* R. Blanchard.

Length 10 meters or more, maximum breadth at anterior end 1.5 millimeters in broadest region 25 millimeters. Proglottides very short, near posterior end only 0.45 millimeters in length by 14 to 16 millimeters in breadth. Head unknown. Genital organs double, two lateral rows of sexual openings on ventral surface located in longitudinal grooves with gen-

ital sinus in front and orifice of uterus behind it. Uterine coils few, extending far lateral; ovary slender, transverse. Eggs brown, thick shelled, 63μ by 48 to 50μ in diameter, with operculum. Found in man in Japan; larva unknown.

Ijima and Kurimoto describe this species as unique not only in the extreme size manifested, but also in the double genital organs. This condition is found in some species from seals, but save for this case is unknown among human parasites. The sexual organs (Fig. 1348) are characteristically bothriocephaline but they are found in double sets right and left in each segment and the orifices open at the bottom of two longitudinal grooves which are striking features in the appearance of the worm (Fig. 1349). Mention has already been made of the suggestion that *Spargánum mansoni* is in reality the larval form of this species.

Fig. 1349.—Ventral View of Portion of Chain from *Diplogonoporus grandis*. *a*, Ventral groove. Natural size. (After Ijima and Kurimoto.)

The patient had suffered for five years from dizziness and colic, which had finally become so severe as to call for his admission to the hospital at Nagasaki. The parasite yielded at once to treatment with extract of male fern, and even on the following day all the trouble of long standing had entirely disappeared. The second case also from Japan passed two specimens of a worm identical with the first; both scolices were lacking here also. All specimens showed fenestration of the proglottides, intercalated segments, and others of asymmetrical form, as in other bothriocephaline cestodes.

The occurrence of related species in seals and whales makes it probable that the intermediate host is a fish and man may be infected by the consumption of poorly cured or insufficiently cooked fish. The parasite is likely to be present in Asiatic immigrants, or to occur on the western as well as the eastern shore of the Pacific. Its occurrence is most likely in northern regions.

A sceond species, *Diplogonoporus Brauni*, has been reported from Roumania by Léon. Two cases are on record and others suspected. In both specimens obtained the genitalia were not developed and the description remains incomplete. The life history and origin of this parasite are absolutely unknown. As in other species this is conjectured to have some fish as its intermediate host.

A related species which is assigned to a new genus, *Braunia jassyensis* has been described also from Roumania by Léon. The parasite is rare and imperfectly known. The discoverer thinks that the larval form came from a fish and reached the human host by chance.

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Cetaceum.—SPERMACETI. "A peculiar, concrete, fatty substance, obtained from the head of the sperm whale, *Physeter macrocephalus* L." (U. S. P.)

This whale is the largest living animal, gregarious in its habits and found in the oceans of both hemispheres, from the extreme north to the tropics. It is hunted for its oil, which is one of the most valuable of its class.

Crude spermaceti is a semi-solid, yellow substance as it is scooped out from its reservoirs, but becomes hard and brittle upon exposure to cold; for purification, it is then pressed in bags, when the oil squeezes through, and the solid *cetaceum* is left behind. This can be further purified by melting in water, skimming, and recrystallizing. Purified spermaceti is a pearly white, glistening, crystalline, translucent, odorless, and tasteless solid, insoluble in water; soluble in ether, chloroform, and boiling alcohol. Melting point 111° to 112° F. It is mostly composed of *palmitic* acid combined with *cetyl* (instead of glycerin); there are also small quantities of compounds of *stearic*, *myristic*, and *lauric acids*. It is fairly permanent in the atmosphere, in this respect excelling most fats.

USE.—Spermaceti has no active medicinal qualities. It is sometimes used in sore throats, etc., where its

value is mostly as a protective. Its principal employment in medicine is as an ingredient of cerates and ointments, to which it gives consistence, blandness, and permanence. Spermaceti is an important constituent of ointment of rose water or cold cream (*Unguentum Aquæ Rosæ*, U. S. P.).

Cetraria.—*Iceland Moss; Lichen Islandicus.* The dried plant, *Cetraria islandica* (L.) Acharius. This is a good-sized terrestrial lichen, with an upright or ascending, long and narrow, leathery, wavy-margined, olive-green thallus, several times dichotomously branched or irregularly fan-shaped, with linear or cuneiform lobes. *Apothecia* shield-shaped, on the upper surface of the thallus. This lichen grows in great abundance on the surface of the ground in open woods and heaths, and on mountain sides, in the arctic and the colder temperate regions of both hemispheres.

It is a valuable pasture plant in the extreme North, and is also employed as an article of human food in parts of northern Europe. Its medical employment is one or two centuries old.

Dried Cetraria is thus described: From five to ten centimeters long, foliaceous, irregularly branched into fringed and channelled lobes, brownish above, whitish beneath, and marked with small, depressed spots; brittle and inodorous; when softened in water, cartilaginous, and having a slight odor; its taste is mucilaginous and bitter.

It should be freed from pine leaves, mosses, and other lichens, which are frequently found mixed with it.

Composition.—About two-thirds of it is *Lichenin* or *moss starch* ($C_6H_{10}O_5)_n$, a starch-like substance, structureless, soluble in boiling water, the solution gelatinizing upon cooling. It is an article of commerce as a gelatinous mass or a white powder. The properties of this substance are purely demulcent. *Cetrarin* or *cetraric acid* ($C_{18}H_{16}O_8$) is the bitter principle, and gives to the drug its slight medicinal properties. It occurs in commerce in white masses of fine needle-shaped crystals, soluble in boiling alcohol, in alkalies, and very slightly in water. It is distinctly stomachic, like other bitters, and antiemetic. It also has the distinct property of increasing the red corpuscles of the blood. It is therefore in an exceptional manner tonic. *Isolichenin* is very similar to lichenin, but gives the starch reaction with iodine. It is apparently not active.

Iceland moss is a very useful demulcent, and has gentle tonic qualities, for which it is indebted to the two active principles above mentioned. It has no specific action upon the bronchi or lungs, and its value in bronchitis, etc., for which it is mostly prescribed, must be due to its combined demulcent and tonic actions. Dose, indefinite; a decoction is official.

Cetrarin is given alone for all except the demulcent properties, in doses of gr. jss–iij (0.1–0.2).

Henry H. Rusby.

Chaillé, Stanford Emerson.—Born July 9, 1830, in Natchez, Mississippi; his father was of French descent. He received his academic education at Harvard College (class of 1851), and immediately afterward began the study of medicine at the University of Louisiana (subsequently named the Tulane University, Louisiana). This institution gave him the degree of Doctor of Medicine in 1853 and his association with the university, thus begun, continued to the end of his long life. In 1858 he was appointed demonstrator of anatomy; in 1867 he was called to the chair of physiology and pathological anatomy and soon thereafter was made Dean of the Medical Department, which position he held uninterruptedly until 1908 when he retired with the title of Professor Emeritus. In preparation for his professional duties he studied physiology (1860–1861), in the laboratory of the eminent French teacher and investigator, Claude Bernard. Soon after the breaking out of the Civil War he returned to New Orleans and entered the Confederate Army. After four years of service in different parts of the South—first as a private soldier, afterward as Surgeon-General of Louisiana, and finally as surgeon in charge of various army hospitals—he was captured and paroled. This was in September, 1865, and a few months later he returned to Paris to resume his studies under Bernard. In 1867 he came back to New Orleans and began his lectures at the University. He was for several years one of the editors of the *New Orleans Medical and Surgical Journal*. He died May 27, 1911.

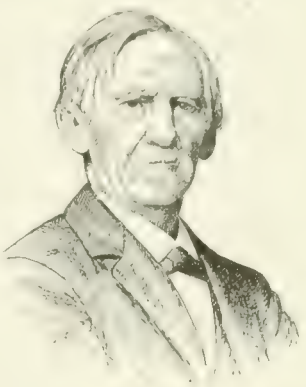

Fig. 1350.—Stanford Emerson Chaillé.

Of the numerous contributions which Chaillé made to medical literature the following deserve to be mentioned: "State Medicine and Medical Organization," Trans. Louisiana State Med. Society, 1879; "Sanitation and Evolution," Trans. Amer. Pub. Health Assoc'n., vol. vi. 1881; "Importance of the Study of Hygiene in Schools," 1882; "Smallpox and Vaccination," 1883.

A. H. B.

Chalybeate Springs.—Meriwether County, Georgia.

Post-office.—Chalybeate Springs. Hotel and cottages.

Access.—Via Atlantic, Birmingham and Atlanta Railroad. The Springs are about seventy-five miles south of Atlanta.

These springs were discovered by Mr. Rawlings about 1835, and opened by him for the reception of visitors a few years later. The improvements were of a rude character until about 1850, at which time they were considerably enlarged. With the exception of a few years' interval they have been open to the public ever since. Analysis by Dr. Eberhart, under supervision of the late W. S. Yates, State Geologist:

One United States Gallon Contains:

Solids.	Chalybeate spring. Grains.	Sulphur spring. Grains.	Magnesia spring. Grains.
Potassium chloride	.222	.245	.140
Sodium chloride	.104	.285	.297
Sodium sulphate	.423	.770	.764
Magnesium sulphate	.350	.....	.....
Magnesium carbonate	1.060	1.656	1.225
Calcium carbonate	1.195	2.907	2.257
Manganese carbonate	.046	.....	.....
Ferrous carbonate	.406	.507	.338
Aluminum sulphate	.157	.....	.....
Sodium carbonate	.....	.467	.397
Aluminum oxide	.....	.052	.097
Silica	1.225	2.193	2.432
Total solids	5.188	9.082	7.949
Free carbon dioxide	2.356	2.074	4.199

The water is a light chalybeate. There are also traces of hydrogen sulphide, crenate of iron, and a

minute trace of nitric acid, lithium, and organic matter. The proportion of soluble silicic acid is larger than usual. This compound is not used in medicine, but silica is contained in the human body, and may not be without therapeutical value. It is possible that the trace of sulphureted hydrogen also slightly influences the action of the water. It has been recommended in all cases requiring a chalybeate water. The flow is abundant, being about twenty-five gallons per minute; the temperature of the water is 60° F. These waters are recommended for stomach, kidney, and bladder disorders, skin diseases, eye troubles, and as a general tonic. Bathing facilities are ample, both hot and cold water being supplied. The climate of this region is of a salubrious character; the altitude is 850 feet above sea level.

EMMA E. WALKER.

Chamælirium.—See *Helonias.*

Chamberlen Family.—A family of British accoucheurs, surgeons, and physicians, famous through four generations for their monopoly of the obstetrical forceps during the first century of its existence. This monopoly rested upon no acquired proprietary rights but solely on concealment, not only of the method of applying the instrument, but even of the very nature of the latter. This family was also distinguished in other respects, such as for the royal favor which they enjoyed—several members having been Court Physicians—and for a tendency to charlatanism which involved them in frequent clashes with the constituted medical authorities; and last but not least for the number of "wild cat" and sometimes malodorous financial enterprises which they sought to promote. Despite these drawbacks hardly any critics dispute their great abilities and the enormous services rendered by them to humanity. In this article we seek only to consider the relations of the family to the obstetrical forceps.

The founder of the family is commonly spoken of as a Frenchman self exiled to England in 1569 on account of his Protestantism. This may be the truth, but does not account for the fact that he had a powerful, near kinsman in London, Thomas Chamberlen, "Master of the Mercers." There is no evidence that he was any sortof a medical practitioner or that he either possessed or originated the family monopoly, nor is there anything to show that he was not familiar with the forceps. His generation is therefore excluded from consideration. The actual first generation to possess the secret represented by his two sons, each called by the same Christian name Peter and known commonly as the "elder" and "younger Peter" (born 1596). The second generation was represented by a son of the latter known as "Dr. Peter" (his father and uncle had never received full membership in the College of Physicians). The third generation was represented by the "first Hugh" (born about 1630), son of Dr. Peter, and in a small way by his brothers Paul and John. The only representative of the fourth and last generation was the "second Hugh" who was son of the first Hugh. The second Hugh toward the close of his long life imparted the secret of the forceps to several medical friends. He was perhaps influenced to this step because in 1723 Palfyn had made public his independent invention of the forceps.

It is commonly stated that we have no proofs of a knowledge of the forceps by the two Peters of the first generation, and that the history of the forceps should not begin with the latter. It was, however, commonly reported in their day that they employed a secret method in delivering women, and it is significant that Peter the elder confined the Queens Anne and Henrietta, in 1614 and 1628, respectively.

Dr. Peter, born 1601, who received the finest academic and professional education possible in his day, and became eminent as both physician and surgeon known to use a mysterious instrument for delivering women and on this account was abused and doubtless slandered. He died in 1683.

The first Hugh at first cared much less for general practice than for midwifery, in which branch he achieved great fame. Some historians would even credit him with the invention or at least the practical introduction of the forceps. He tried to sell the secret to Mauriceau (whose treatise on midwifery he translated into English) and actually did sell it to Roonhuysen, but the latter seems never to have used it and is therefore believed to have been swindled.

The second Hugh was distinguished both as general practioner and accoucheur, and seems to have been without the failings of his predecessors. As already stated, he allowed the secret of the forceps to become public. A kinsman named Walker claimed to retain the family monopoly but the instrument soon came into general use.

The Chamberlen forceps is described under *Forceps.* Some of the instruments actually used by the family have been preserved. It is commonly spoken of as a low forceps with no pelvic curve and the wonder is that so much was accomplished with so primitive an apparatus.

EDWARD PREBLE.

Chamomile.—See *Anthemis.*

Chamomile, German.—See *Matricaria.*

Chamomile, Spanish.—See *Pyrethrum.*

Chancre.—See *Syphilis.*

Chancroid.—Chancroid is a local contagious, venereal disease, consisting of suppurating ulcers on or about the genitals, generally with inflamed lymphatics leading to swollen or suppurating glands in the immediate vicinity.

The disease arises from contact with secretions from like lesions, and while its course may be severe, destroying large areas of tissue, it still remains a local process never causing constitutional infection. Formerly syphilis and chancroid were classed together as "The Venereal." Bassereau in 1853 established the fact that clinically the diseases were separate and distinct, each with its natural history and running its peculiar course. In 1889 Ducrey described a bacillus as the cause of chancroid. His claim was verified by Krefting, Unna, Mallory, and others.

Schaudinn and Hoffman in 1905 demonstrated the *Spirochæta pallida* as the cause of syphilis. Previous to their discovery, the diagnosis rested on a foundation built up almost entirely of clinical observations; the microscope and animal experimentation having been of no service until 1903, when Metchnikoff and Roux successfully inoculated a female chimpanzee with fresh scrapings from a syphilitic chancre. This achievement was of value in verifying the clinical observations on the long incubaton period of syphilis, a most important fact in the diagnosis of chancroid, which has practically *no* incubation period, the sores appearing a few hours or days after exposure and continuing to spread by autoinfection for some time.

Too much emphasis cannot be placed on the importance of a careful examination and accurate diagnosis of all genital sores, as extreme penalties are frequently exacted in case of error. Either of the following mistakes often occurs: a patient is told he has simply a local sore and is allowed to marry, carrying syphilis to his wife and offspring—or the patient with syphilitic chancres and an acquired phimosis is considered by his doctor to have chancroids and circumcision is advised to expose the soft sores. It is impossible to estimate how many surgeons infect themselves with syphilis in performing this unnecessary operation, where the true condition is unsuspected.

Chancroid is less common than syphilis at the present time, a fact not generally appreciated. During the years immediately following our Civil War and to a less marked degree, the Spanish War, chancroid was much more prevalent, partially due, no doubt, to lack of personal cleanliness on the part of the men and the camp followers.

To the clinical observer the purulent secretion from chancroids is the medium which conveys the contagion.

Cold is said to have little if any effect on the vitality of the organism, while it is readily destroyed by drying, heat, and antiseptics.

Etiology.—Chancroid is undoubtedly due to a specific microorganism, and now the streptobacillus of Ducrey is accepted as the etiological factor of the true chancroid, but the name, chancroid, is still applied to all suppurating local lesions about the genitals, whether due to the streptobacilli or the common pyogenic bacteria. Undoubtedly this accounts for the lack of uniformity of descriptions and microscopical findings.

There are presumably, widely different varieties of chancroids described by various authors. This being the case, it seems reasonable that there should be a difference in their character also, due to different causes. This explains why one finds only pus organisms and another the organism of Ducrey from presumably the same sort of sores. In reality they are examining different kinds of ulcerations. In other words, certain lesions are called chancroid, which if they occurred on the body would be called staphylococcia, while others, with a much greater tendency to extension and destruction would show the streptobacillus of Ducrey. Such cases have been observed side by side. Post (*Jour. Boston Society Med. Sciences*, vol. v., No. 4, 1900) reports two cases under his care at the same time, each the result of contagion and each diagnosed as chancroid. The first case was a gangrenous sore which destroyed a large portion of the true skin of the prepuce resulting in a ragged circumcision. Bacteriological examination showed only the ordinary pus cocci and aside from its extremely destructive nature it was in no way peculiar. In the second case the original sore was situated on the reflected prepuce. Before coming under Post's care the sore had been cauterized in the hope of accomplishing its complete destruction if it was chancroid. It was not destroyed, and to quiet the patient's fears, his doctor resorted to autoinoculation to determine its true character. This inoculation was made about half way up the shaft of the penis. Within forty-eight hours a pustule appeared which spread slowly but surely, chiefly subcutaneously, the sloughing of the skin being secondary to the destruction of the subcutaneous tissue. In various places it travelled through the subcutaneous tissue for nearly an inch before coming to the surface. This process of healing in one spot and advancing in another continued until the skin over nearly half the circumference of the penis was destroyed. The nearby lymph glands suppurated and sloughed and these ulcerations showed this same tendency to extend. The original sore healed promptly, but the one resulting from the inoculation lasted nearly three months and from this lesion the bacilli of Ducrey were demonstrated.

Opposed to the followers of Ducrey are those who claim chancroid is simply a manifestation of infection with the ordinary pus-producing organisms. It has even been stated that cases have arisen *de novo* there being no active chancroid lesions present in the party giving the infection.

In asserting that soft sores are of purely pyogenic origin, it is claimed that secretions from chancroids always show the presence of streptococci, staphylococci, and non-pathogenic bacilli as well as the streptobacilli of Ducrey. It is claimed that chancroid is to mucous membranes what impetigo is to the skin, and that streptobacilli are an accidental accompaniment and not the cause. Furthermore chancroid is said to be more often found in prostitutes physically below par and among the poorer classes, the type of individual whose vitality is lowered by improper food, overindulgence in alcoholics, general unhygienic surroundings, and lack of personal cleanliness. In short, a class with diminished resistance where slight abrasions would easily become infected with pus cocci, suppurate freely, and do badly in general. Certainly the genitals in the uncleanly, with warmth, moisture, and decomposing smegma, furnish an excellent medium for the growth of pus organisms.

Unfortunately for the pus cocci theory of the origin of chancroid, the disease is by no means confined to the debilitated but may occur in the robust when exposed to the chancroidal infection.

If pyogenic bacteria alone are responsible for producing soft chancres, then individuals with long foreskins and decomposing smegma or excoriative balanitis, causing acquired phimosis with foul subpreputial discharge would develop these lesions. Furthermore, females with periurethral and vulvovaginal abscesses occurring during the course of gonorrhea, and men with excoriations dependent upon scabies of the genitals would also develop chancroid. Clinical experience shows that such is not the case. Ulcerations, undoubtedly the result of pus infection, occur about the genitals, due usually to a staphylococcic infection of abrasions or excoriations and run the same course as similar impetiginous affections of the skin. The Ducrey bacilli are much more destructive in their effect upon the tissues in depth as well as in extent and heal with the formation of permanent scars. It was pointed out by Ducrey that in repeated inoculations from true chancroid lesions the accompanying streptococci, staphylococci, and other bacteria disappeared from the lesions having nearly pure cultures of his streptobacilli.

Bacteriology.—According to Muir and Ritchie the streptobacilli of Ducrey are minute oval rods slightly thicker at the ends, 1.5 μ in length, and 0.5 μ in thickness. They are found mixed with other organisms in the purulent discharge and are arranged in small groups and chains. Sections through the floor and walls of the ulcer give the best idea of the arrangement in chains. They are situated deeper than other organisms and are found in nearly a pure state among the infiltrated leucocytes. They are usually free but may be within the cells.

These bacilli have been found in pure culture in many cases of chancroidal buboes both by microscopic examination and by cultures, negative results of some observers being due to the organisms having died out.

The weight of evidence shows the bubo associated with chancroid to be another lesion of the bacilli of Ducrey. Sometimes contaminations with the ordinary pus organisms occur.

The bacilli stain quite readily with the ordinary aniline stains but decolorize rapidly. Smear preparations requiring no dehydration can be easily stained with Loeffler's or Kuhne's methylene blue. These are preferable because they do not overstain. With sections great care must be taken in the process of dehydration and the aniline-oil method should be used, as alcohol quickly decolorizes the organism. A little methylene blue may be added with advantage to the aniline-oil used in dehydration.

Cultivation.—For a long time attempts at cultivation were unsuccessful. However, within recent years Benzançon, Griffin, and Le Sourd obtained pure cultures in four cases. They used a mixture of rabbit's blood and agar; one part of the former to two of the latter. The blood is added to the agar when melted at 45° C. and the tubes slanted.

Davis confirms these results and states that freshly drawn human blood distributed in small tubes is a good medium. This medium is of especial value as the blood inhibits the growth of extraneous organisms.

On solid media (blood-agar) the growth appears as small round globules, attaining complete development in forty-eight hours, having then a diameter of one to two millimeters. The colonies do not become confluent. Under the microscope these colonies show appearances similar to those seen when the organism is in the tissues. Occasionally long undivided filaments are found which Davis regards as degenerative forms.

Cultures undergo marked degenerative changes in a comparatively short time, and great irregularities of form and shape are found. A relatively large amount of blood seems necessary for their growth, and even subcultures in the ordinary media including blood serum give negative results. No results are obtained by inoculating the ordinary laboratory animals, but it has been found that some monkeys are susceptible, it being possible to produce small ulcerations by superficial inoculation, the organism being demonstrated in these ulcerations.

Tomasczewski cultivated the bacilli for several generations and reproduced the disease by inoculation of the human subject.

Muir and Ritchie conclude: "The causal relationship of this bacillus (to chancroid) must therefore be completely established, and the conditions under which it grows show it to be a strict parasite, a fact which is in conformity with the known facts as to the transmission of the disease."

Unna gives a very clear description of the origin of the chancroid lesion as follows: The bacilli enter through a break in the skin or mucous membrane, and cause a small epidermal pustule which is quickly followed by shedding of the whole epidermis. The bacilli spread in radiating lines along the lymph vessels into the skin which is infiltrated with large numbers of plasma cells on account of the active toxicity of the organisms. The skin is quickly undermined and the bacilli penetrate into any fragments of tissue causing necrosis. Living bacilli are found chiefly in the outer zone of infiltration near the healthy tissue. They die off along the surface and in the areas of necrosis.

Clinical History.—The time between inoculation and the appearance of the soft sore is so short (twenty-four to forty-eight hours) that one can hardly speak of it as a period of incubation. This is the first striking difference between chancroid and syphilis, with its long stage of incubation.

The lesion is said to begin as a minute papule with a yellowish vesicle in the center having a slight zone of redness and inflammation about it. It increases in in size usually quite rapidly, and the vesicle ruptures leaving a small round or oval-shaped ulcer with a gray velvety uneven base. The edges are sharply defined giving it a punched out appearance. In true chancroid the edges soon become undermined, the ulcer extending in this manner, and the extension may be extremely rapid. This rapid extension and deeper destruction form one of the striking contrasts between lesions caused by Ducrey bacilli and the ordinary pus cocci. The chancroid ulcer secretes pus freely. The base is dotted here and there with small red points which bleed very easily on rough handling or in removing dressings that have been allowed to stick. This is a striking difference from the chancre of syphilis which shows little tendency to bleed. Whether the lesion is single or multiple at the beginning, fresh points of infection soon appear, the process spreading more or less rapidly by autoinoculation, the lesions passing through the various stages of development and repair. This tendency to spread by autoinfection is one of the striking and constant characteristics of the disease. Syphilis is never autoinfectious. The floor and margin of a chancroid ulcer is never indurated except as the result of cauterization in an attempt at its destruction. Generally within a short time after the ulcers appear the lymphatics and nearby glands show a painful inflammatory swelling; usually but a single gland in the chain is involved. The skin over the swelling soon takes on a pinkish hue, then a deep red, and finally a dark reddish purple or even a bluish tint, hence the popular name with patients, "blue balls" or "blue boys" (buboes). Ordinarily the glands in one groin only are affected but both may be inflamed. Frequently the glands break down and require surgical care. In determining the character of a doubtful sore careful notice should be taken of the character of the nearby lymph glands, for their behavior is so totally different in chancroid and primary syphilis, as to be of great value in making a clinical diagnosis. The old saying, "soft sore, suppurating bubo; hard sore, non-suppurating bubo," is as true to-day as when the observation was first made.

In men with long foreskins, chancroids situated on the mucous membrane of the prepuce or along its free margin often cause an acquired phimosis which tends to retain secretions causing septic absorption as shown by the local heat, redness, swelling, and pain. The whole prepuce may feel thick and brawny and the edema cause considerable deformity of the organ. As the process advances there is a more or less profuse thin purulent discharge from the ostium preputii, which at times suggests a gonorrhea. The microscope easily determines this point. One can usually make out the dorsal lymphatic in these cases as a hard tender cord leading to a small gland at the base of the penis. When chancroids are situated at the ostium all attempts at retracting the foreskin are painful and cause more or less stretching of the lesions and some bleeding. Micturition causes much smarting as the urine must traverse these raw surfaces. This pain can be somewhat lessened by immersing the penis in warm water while urinating.

Location.—Chancroids are usually situated about the genitals. Extragenital lesions may occur but are rare compared with the extragenital primary sore of syphilis. When extragenital chancroids are found they are due to the transference of secretions by the hands of careless patients. In men soft sores are most often situated in the sulcus back of the glans, especially near the frenum along the mucous membrane of the prepuce to its junction with the skin; at times on the skin itself. At the frenum minute tears occur from mechanical violence during coitus and are readily infected. Ulcerations here generally perforate and destroy the frenum. These lesions are painful, bleed easily, at times quite extensive hemorrhage may occur, and healing is often slow. In women the lesions are situated about the introitus vaginæ, clitoris, and the labia or even on the upper part of the thighs and about the anus; rarely if ever on the cervix uteri or the walls of the vagina. The number of lesions in any case is variable. They are generally multiple but may remain single. The multiplicity is due to the autoinfectious character of the secretions. The bacteria can undoubtedly penetrate sound mucous membrane when deposited thereon, while entrance through the skin is gained by the way of minute abrasions or hair follicles.

The power of autoinfection is perhaps best seen in the case of females who are careless about personal cleanliness and allow secretions from their sores to run over the area about the genitals resulting in new foci of infection.

In determining the character of a doubtful sore it was formerly common to test its autoinfectiousness. The microscope is now used instead and is quicker and free from danger. However, if this old time test

is made, a spot well removed from large chains of lymph glands should be selected.

In size chancroids vary from a pea or smaller in mild cases to a silver dollar or larger where lesions run together, or are of the phagedenic type. The size of the lesion is of comparatively little importance in making a diagnosis. In shape the ulcer is most often rounded or oval. Severe chancroids run a tedious course, modified somewhat by the patient's general physical condition and habits of life as well as the medical care. There is no tendency toward running a self-limited course. Too strenuous exercise, indulgence in alcohol, and complications like phimosis, suppurating buboes, gangrene, and phagedena may prolong the case indefinitely. The course of the disease may be divided into three stages: The period of destruction followed by a variable length of time in which the process seems to remain stationary, and then the stage of repair. The ulcers appear more healthy, necrotic tissue if present sloughs away, healthy granulations spring up in the sluggish gray base of the ulcers, and healing by granulation occurs, leaving a permanent scar where there had been a loss of tissue.

Differential Diagnosis.—Chancroid is to be differentiated from pustular lesions accompanying scabies of the genitals, herpes progenitalis, the primary lesion of syphilis, syphilitic mucous patches, particularly in women, ulcerated papules, and ulcerating gummata.

Scabies is diagnosed by the presence of burrows and evidence of scratching about the privates as well as signs of scabies on other parts of the body. Pustular lesions of the glans in these cases are simply an infection with pyogenic bacteria. The condition is seldom severe, rarely causing glandular enlargement, while itching is a prominent symptom.

Herpes progenitalis should rarely if ever be mistaken for soft chancres, inasmuch as they occur regardless of exposure and are generally preceded by a sensation of burning and itching. The eruption appears as a group of minute vesicles which rupture so easily that they often are broken before being seen. The condition first noticed is a small erosion of the mucous membrane. The lesions may gain considerable size by the coalition of several vesicles. They secrete serum rather than pus and there is rarely any glandular involvment. The disease runs a self-limited course of from a week to ten days. Certain individuals are prone to repeated attacks. Cases of simultaneous herpes of the genitals and of the lips occur but with no great frequency. The attack in itself is of slight importance. However, much mental anguish may be caused the individual who is leading an irregular life. Cases of primary syphilis occur where the virus finds entrance through an herpetic lesion. All but one of the spots heal in the usual time, this one fails to do so, or if cured reulcerates and assumes the characteristics of an initial lesion of syphilis.

The Primary Sore of Syphilis.—Recent years have given valuable aids in the differential diagnosis between hard and soft chancres. As we have seen, laboratory methods and tests are uncertain and of little help in making the diagnosis of chancroid. This is not the case with the primary lesion of syphilis. However, one should study the clinical signs carefully and look to the laboratory only for confirmation of the diagnosis, not the diagnosis itself. It is still possible to make correct clinical diagnosis in a large majority of these cases. The term chancroid is still used to designate all non-syphilitic ulcerating lesions about the genitals, whether due to pus cocci or the bacillus of Ducrey.

Chancroid has a short incubation period; chancre three to four weeks; chancroid is autoinoculable; chancre is not; chancroid has an inflammatory bubo, often going on to suppuration, while the buboes of syphilis are non-inflammatory and seldom break down. Chancroid is an ulcerating destructive process free from the firmness known as induration while the chancre is an erosion on an indurated base; a constructive lesion, a new growth due to the infiltration of round cells. The base of soft chancre is uneven, of a dirty gray color, showing bleeding points especially on handling. The edges of the sore are undermined and the process may extend over quite large areas, healing with scar formation. The erosion of chancre shows little tendency to bleed or extend and when resolution occurs often leaves little or no scar, especially on mucous membranes. Chancroid is never followed by constitutional manifestations as is the case with syphilis. As has already been stated the laboratory aids to diagnosis in soft sores are uncertain, the Ducrey bacilli being rather difficult to demonstrate in smear preparations and their cultivation is still more uncertain. With syphilis, however, it is usually fairly easy to demonstrate the presence of *Spirochæta pallida* in primary lesions, in stained smear preparations, or the spirilla are seen motile in serum with the dark stage microscope. The Wassermann reaction is another aid of great value in the early diagnosis. The reaction usually becomes positive by the third to sixth week in nearly 100 per cent. of the cases. Noguchi's luetin skin reaction is of value chiefly in the later stages of the disease, where it gives a high percentage of positive results, higher than the Wassermann. This test is similar to the von Pirquet tuberculin skin reaction. Hence, with the Wassermann for early and the Noguchi for late cases we have tests of much value in making differential diagnoses.

The *mucous patches* or ulcerated papules of secondary syphilis, especially when occurring about the vulva and anus in women, are at times mistaken for chancroids. These lesions, however, have a thin serous secretion instead of pus, are seldom ulcerations like soft chancres, and lack the accompanying inflammatory lymph glands. There is also a lack of incubation period and further examination of the patient will probably reveal other signs of syphilis. The finding of spirochetes in these lesions and a positive Wassermann will reveal the true nature of the condition. Secretions from these mucous patches are foul smelling and highly contagious but never autoinfectious. At times a late specific ulcerating papule or gumma may occur about the genitals and simulate chancroid or even the primary lesion of syphilis very closely. There is no history of exposure, no enlargement of glands, or autoinfection, the blood test probably positive, and a history of preceding syphilis. Testimony to this in the shape of scars, periosteal swellings, or trouble with eyes, ears, or nervous system is usually to be found by careful examination and questioning.

A *periurethral abscess* most frequently occurs in the sulcus near the frenum and might at first suggest a chancroid, but if its sharply circumscribed appearance and inflammatory character are noted together with the history of a previous gonorrhea, a correct diagnosis is easily made.

Complications.—The complications of soft chancres are phimosis, paraphimosis, lymphangitis, suppurating bubo, gangrene, and phagedena; fortunately, the two latter are seldom seen nowadays.

Phimosis and *paraphimosis* are not infrequent. In phimosis the whole prepuce may become swollen, hot, red, tender, and edematous. There is a varying amount of subpreputial discharge and often a series of chancroid lesions about the ostium preputii show the character of the sores within. Occasionally in severe cases where the swelling is extreme and unrelieved, the ulcerations extend through the prepuce allowing the glans to protrude, thus relieving the tension by a spontaneous circumcision. Paraphimosis is less common, but often a more painful complication. It is usually the result of retracting a tight

foreskin for purposes of cleanliness, and congestion of the glans from constriction prevents its return. Swelling, inflammation, and edema occur accompanied by much pain and deformity, the constriction in the sulcus at times causing the end of the penis to point at nearly right angles to the shaft. If the paraphimosis is not reduced within a short time, an ulceration at the point of constriction occurs, which is nature s method of relief. These ulcerations frequently become infected with the chancroidal pus and extensive destruction of tissue may result.

Treatment.—There is no specific drug, vaccine, or antitoxin in the treatment of chancroid. It is essential that the patient keep as quiet as possible, avoiding all excessive exercise like skating, dancing, running, lifting, etc. This somewhat lessens the danger of suppurating bubo. Cleanliness is of the utmost importance. This is best accomplished by the free use of soap and water, followed by antiseptic solutions, which should be used as hot as is compatible with the patient's comfort, as heat in itself is beneficial. Hence prolonged hot soaks or the application of hot compresses play an important rôle in the treatment. Formerly it was almost the universal custom to cauterize these sores, and various agents were employed such as sulphate of copper, popularly known as "bluestone," nitrate of silver stick, nitric acid, acid nitrate of mercury, and many others. Their use accomplished little good and seemed to be followed by more suppurating buboes than occur with less radical measures. Happily caustics are in little favor to-day. If a sore is sluggish and needs stimulating, touching it with ninety-five per cent. carbolic acid, followed by alcohol, seems to accomplish best the desired result. This is an attempt to change a sluggish ulcer into a healthy, granulating sore. The pain from this procedure is slight owing to the anesthetic effect of carbolic acid.

Following the cauterization a bland, moist dressing should be applied for a few hours. Lead wash or boric-acid solution acts well. Later, this treatment should be changed to some soothing powder—boric acid, aristol, calomel, iodol, or acetanilide. The same treatment is applicable to both males and females, but it is more difficult to keep lesions clean and the dressing applied in the latter. Probably no single drug is more efficacious in these cases than iodoform, but its odor greatly restricts its use.

Generally speaking ointments are of less value in the treatment of chancroids than washes and powders.

The principal antiseptic solutions in use are saturated boric acid, creolin 1 to 25, carbolic 1 to 50, lysol 1 to 50, corrosive sublimate 1 to 2,000. In their use care must be exercised to avoid dermatitis.

The stick of silver nitrate, popular with the laity as a caustic, is of little value as its action is superficial, irritating, and especially apt to be followed by suppurating lymph glands. Its only use should be in stimulating small areas of sluggish granulations. Caustics should never be applied to a sore that cannot be thoroughly exposed and properly cared for.

As a rule internal medication is not needed unless the patient is much reduced in strength, in which case general tonics, such as iron, quinine, cod-liver oil, hypophosphites, combined with fresh air, diet, and general hygiene may be of service.

Mercury should never be given in cases of chancroid as it negatives the Wassermann reaction, which might be of help in the early detection of syphilis complicating chancroids. With good care and cooperation on the part of the patient, the disease should run its course in two to six or eight weeks, unless extended by complications.

C. Morton Smith.

Change of Life.—This term, in common use, signifies the series of phenomena which are apparent at the end of the child-bearing period. It is applied exclusively to women, though an analogy has been observed between some of the conditions which affect women at the period in question and similar conditions which have frequently been noted in men at the time when their physical powers have reached their culmination. The term which is generally accepted and used by medical writers as correlative with *change of life* is *menopause*. This term is sufficiently explicit for only one link in the chain of phenomena which comprise the *change of life*, to wit, the cessation of the monthly flow. For this reason the common term is the more exact and comprehensive and therefore presents claims for its general use.

The change of life is really one of the great epochs in the life of woman, for it not only serves as the boundary line between the period in which she is able to reproduce herself and her species—period of fruitage—but it marks the limit of the progressive stage of her physical condition in general, deterioration being henceforth the prevailing process, whether it develops slowly or rapidly.

Time of Occurrence.—Like all the other functions of animal life, this one also is subject to great variations as to both the time of its occurrence and the events which characterize it.

According as it occurs early or late in life it may be premature, normal, or retarded, and it may be natural or artificial according as it is or is not solely the product of physiological forces.

In temperate climates we may expect its appearance in the majority of cases between the fortieth and forty-fifth years; family or race peculiarities may advance it two or three years or defer it for an equal period. It is premature when it occurs prior to the fortieth year and it is retarded when it occurs later than the fifty-fifth.

Influences which Modify its Occurrence and its Course.—*Race.*—The nearer a tribe or race of human beings approaches the lower animals in its intellectual development the less marked will be the menstrual function in its women.

Menstruation is quite clearly the development or evolution of the *rut* or *estruation* in the lower animals. In the apes and monkeys we observe very frequently a distinct regularity in what may be termed for them the menstrual flow. Neither in the animals nor, so far as my knowledge extends, in the lower orders of human beings are there well-defined conditions which might constitute the change of life, at least as this experience is observed in the more advanced races.

In proportion as a community or race advances in civilization do we see the menstrual function and the change of life assume distinctness and character. While it does not follow that their unusual or pathological features are necessarily the result of civilization, since there are countless examples in which no appreciable disturbance is experienced from either, it is certainly true that such disturbance does accompany civilization.

Climate.—The influence of extremes in temperature acts upon the change of life precisely as we would anticipate. In the tropics vegetation is luxuriant, matures early, and is profuse in its fruitfulness, but the duration of its life is shortened by the very excess of this profuseness. It is the same, to a certain extent at least, with human females who are native to the tropics: they mature and bear their children early, and in frequent instances reach the menopause between twenty and thirty. This has been observed especially of the Arabs of the desert. To the Caucasian races transplantation to the tropics means a distinct lowering of vitality, with a great diminution in reproductive power and a consequent tendency to the early cessation of the menstrual function, and the advent of the change of life. In the Arctic regions the effect of extreme cold upon vitality is similar to the effect of extreme heat, though it may be made endur-

able to a greater degree than the latter. The natives of the Arctic regions are stunted in form and more or less deficient in vitality. This is especially the case after they have endured the rigors and the darkness of the long Arctic night. The women seldom mature earlier than the twentieth year, menstruate very infrequently, and seldom have more than one or two children. The duration of life is not great, and the change of life comes between thirty and forty.

Altitude.—The significance of this factor is due, of course, to the change in the air pressure. Women may gradually become habituated to any condition of atmospheric pressure, but the effects which obtain prior to such habituation are very distinct. A change to the sea level by one who has lived away from the sea and at more or less of an elevation generally suspends or otherwise disturbs the menstrual flow, and in cases in which there is decided constitutional disturbance it is possible that the change of life might be hastened by such residence.

Those who go from the sea level to reside at altitudes of 6,000 to 7,000 feet or more experience, on the other hand, increased profuseness in the menstrual flow, the external air pressure being greatly reduced. Of the influence of such reduced pressure upon the change of life except in prolonging its duration and increasing the frequency and profuseness of its hemorrhages, I am not prepared to speak. I know of no statistics bearing directly upon this subject, which is one of the many fruitful themes in climatology still awaiting investigation.

General Physical Condition.—The general condition of a woman has much to do with the inauguration of the change of life and with the events by which it may be characterized. Those who suffer with grave constitutional and visceral diseases which seriously impair their vitality are almost certain to experience an arrest of menstruation and often other symptoms which accompany the change of life. Those who suffer from tuberculosis, syphilis, general anemia, chronic diseases of the liver or kidneys, etc., are in this category. The acute wasting diseases sometimes produce so profound an impression that the menstrual function is entirely obliterated. On the other hand, the malignant diseases of the genital organs, if present at a time when the change of life might be expected, cause its unlimited delay. I do not recall a case of such disease, in a very large experience, in which the change of life ensued after the malignant disease had begun its destructive career. In fibroid tumors of the uterus, especially those which are characterized with much discomfort and hemorrhage, it was formerly the custom to hold out the hope that all trouble would cease when the change of life brought its beneficent issue. In most cases this has proven the most unsatisfactory will-o'-the-wisp hunting by which a poor mortal could be deluded. The change of life again and again escapes the grasp, until finally it comes to mean that transformation which arrives for us all "when this mortal shall have put on immortality."

The beneficent influence of modern gynecology has removed the veil of ignorance in regard to this subject, and the early removal of these tumors has alike brought on the change of life and the relief of many troublesome symptoms. The change of life comes quite early in women who become excessively fat. Such women are usually sterile. Their physical condition unfits them for the normal experiences of pregnancy and parturition, menstruation is infrequent, scanty, and painful, and it is not unusual for the change of life to occur within a few years of the appearance of the obese condition.

Surgical Procedures.—Certain surgical operations are conducted with the deliberate intention and purpose of bringing about the change of life. Such are all operations in which the ovaries are entirely removed. It is estimated that in ninety per cent. of cases of removal of the ovaries menstruation is at once arrested. If the uterus and Fallopian tubes are also removed the percentage in which such a result is obtained will be even greater. There are no other surgical procedures which act so directly to induce the change of life as does extirpation of the ovaries. Operations which may be followed by prolonged suppuration and invalidism, by impairing the general nutrition and reducing vitality may result in arresting menstruation temporarily or permanently and in bringing about the premature appearance of the change of life.

Occupation.—Both a direct and an indirect influence may be exerted by occupation upon the subject which is under consideration. Such occupations as keep a woman in an elevated temperature during most of the day are very disturbing to the menstrual function, have a very decided tendency to produce obesity, and may induce the change of life prematurely. Cooks, laundresses, and bakers are particularly subject to such influences. Other occupations which impair nutrition and vitality also disturb the menstrual function and hasten the change of life. Workers in chemical factories and laboratories upon arsenic, copper, lead, phosphorus, and other poisonous substances, workers in mines, cellars, in badly lighted, badly ventilated, and damp surroundings are included in this category. Other sufferers are those whose work is exhausting and unwomanly and predisposes to wrinkles and premature old age; such are fishwives, field workers, bearers of heavy burdens on the shoulders or head, mechanics' assistants who may carry tubs of mortar, casks of water or other heavy burdens, all these being types of laborers which one sees much more frequently among the laboring classes in Europe than in this country.

Excessive Fertility.—With many women the reserve capital of vital force is not large. Bearing children in rapid succession until five, six, or more have been borne in as many years exhausts that capital, and then follows the change of life while the woman is yet young. The reason for this is perfectly plain and is seen in the results which follow over-productiveness in animal or vegetable life wherever we may take the trouble to investigate it. Such a result can hardly be regarded as disease, but simply as the taking up of a certain amount of capital to which nothing remained to be added by way of replenishment.

Dissipation and Vice.—The number of women who lead irregular and vicious lives is so great that it would seem as if important deductions might be made from the study of such lives. It has happened in my experience to see quite a large number of women of the vicious and depraved class of all ages. These women suffer greatly from both acute and chronic diseases of the pelvic organs; they frequently suffer from profuse hemorrhage from the uterus, and their excesses very often result in sterility, so that if the vicious life is followed by marriage, it is not likely to be a fruitful marriage. It has been a matter of surprise to me, again and again, that the excesses in sexual intercourse on the part of prostitutes and others do not arrest menstruation and bring on the change of life. Of course irregular habits, late hours, excesses in alcohol, etc., frequently break down the health, and the menses may be arrested as the result of anemia, etc., if the woman does not die promptly from exhaustion or some acute disease, as is the result with many. As a matter of fact I have seldom been called to record such an occurrence; indeed, the stimulation of the sexual organs and the careless, irresponsible life of many of these women seem to improve nutrition, and for a long time, at least, their physical condition is surprisingly good.

Phenomena and Duration.—There are certain phenomena which are almost invariable and others which are only occasional to the change of life. We

must also remember that with some women the transition is immediate and without appreciable symptoms, except that the ordinary monthly flow abruptly ceases. The leading symptoms are practically the same whether the condition is the natural change or one which is induced by disease or surgical procedure. To those who experience it while still far removed from the usual period of time when it is to be expected, the symptoms may be exaggerated; but not necessarily so, for I have seen young girls go through this change with scarcely any discomfort or unusual happening.

Cessation of the Menstrual Flow.—The leading symptom is the disappearance of the regular monthly bloody discharge. This cessation may occur abruptly, the flow appearing one month, disappearing the next and never reappearing. This may be explained by the fact that physical maturity has been reached, just as the fruit falls from the tree when it is ripe; or it may be the result of disease, of removal of the ovaries, of intense emotion, etc. If the cessation of the menses occurs in young women, the possibility of its restoration in due season must be considered. Instead of an abrupt cessation the flow may reappear at regular or irregular intervals, two months, four months, six months or longer, finally ceasing altogether after one, two, or three years.

Excessive Flowing.—A very marked feature in some cases, when the flowing has become irregular, is its profuseness. It was formerly thought proper to do nothing for this symptom on the supposition that it was simply a natural discharge. I have striven diligently for years to combat this view. Excessive loss of blood is always unusual, abnormal, and should be investigated and arrested. The condition of the uterine mucous membrane usually calls for active treatment in such cases by the application of astringent substances to it or the removal of granulation tissue, which may be the cause of the hemorrhage, by the curette. Tumors and other disease of the uterus assume particular importance at this time, and one should never leave to the unaided efforts of nature the disposal of a burden at this time which she may be unable to dispose of or only with great risk to the patient's life.

Flushing and Other Vasomotor Disturbances.—Almost as common a symptom as the arrest or irregularity of the menses is the vasomotor disturbance which occurs without warning many times a day until toward the end of the change, and is manifested now by flushing and heat, and now by pallor and chill. The experience of each paroxysm may continue but a moment, but it is annoying and in some cases depressing and weakening. What should cause this peculiar vasomotor influence, now paralyzing and again stimulating the vascular system, can be only a matter of conjecture. It is an experience which is so universal that it may be regarded as not far removed from the physiological. It is one of the first symptoms which occur, it continues two or three years, and by that time it has become endurable by its very frequency. With some women it continues uninterruptedly to the end of life. It seems to make no difference whether the menopause is natural or induced as to the frequency and intensity of this symptom. It may be expected, however, that with those to whom the change comes early in life it will continue longer, as a rule, than with those to whom it comes as an entirely natural experience.

Mental and Nervous Phenomena.—One of the many notions concerning the change of life which formerly prevailed was that since it was a *critical* time all sorts of unpleasant things might be expected to develop in connection with it. If a woman became crazy at that time it was the change of life which did it, and it was more than likely that she would become crazy if she had any predisposition or predilection to mental instability.

The arrest of the menses and the disturbance of the blood tension undoubtedly may cause brain disorder in those who are predisposed to such trouble, and this may vary in its manifestation between headache and violent delirium terminating in mania or melancholia. Many women are *queer* or unusually hysterical at this time, neuralgias of all varieties are frequent, insomnia is not infrequent, and a disposition which has heretofore been amiable may be suddenly or gradually transformed into one to which the most unusual or grotesque desires or actions are possible. The outbursts in such cases should not all be attributed to the change of life, they are due in part to the previous inheritance of the individual and in part to the tissue changes which take place. Besides, the great majority of women have none of these experiences at all, so that they must be considered exceptional and not a customary accompaniment.

Changes in Nutrition.—Changes in nutrition are a noteworthy feature of this period, the active upbuilding time of life is over, and the tissues now and henceforth are less substantial. Muscular tissue tends to degenerate and atrophy, and fat is accumulated. This may lead to improvement in the general appearance and rounding of the figure, but it may also lead to grossness and obesity. Personal beauty is lost in some cases while an unusual attractiveness is acquired in others.

This period and the remaining years of life being the era of degeneration, it is not strange that cancer of the breast, the womb, and other genital organs should be found at this time more frequently than in earlier life. Cancer is not necessarily a feature or customary accompaniment of the change of life. This is a fact which I have insisted upon for years in spite of a prevalent opinion to the contrary, both in the profession and in the laity. It frequently coexists simply because the change of life stands at the entrance of the degenerative period. We look for cancer in men in its greatest frequency at the same period of life that we look for it in women; the ending of the child-bearing period and the cessation of the menses must therefore have little to do with the development of malignant disease.

Disturbances in Various Organs of the Body.—These have been frequently noted, and in a book which was written by me upon this subject ("The Menopause," D. Appleton and Co., 1897) various complicating affections have been alluded to. It has always seemed to me very necessary that one should carefully distinguish those complications which merely coexist from those which cause or are caused by the change of life. Dimness of vision has been reported as an accompaniment in many cases, also liver engorgement or other derangements in efficient working power of the kidneys and urinary bladder, loss of appetite, indigestion and constipation, rapid action of the heart and dyspnea. These, it will be observed, are all functional disturbances, and it is such rather than organic lesions of which the change of life is most likely to be the cause.

Impregnation after the Change of Life has Occurred.—The question is an interesting one, and it has often been asked whether impregnation could occur after the menstrual flow had entirely ceased. This question may be regarded as entirely settled, indeed it may be said that impregnation has very little to do with the menstrual flow or the menstrual flow with it. It is said that the Esquimau women are impregnated customarily before the menses have appeared. Many instances have been observed in which a similar event has occurred in our own latitude before the appearance of the menses. The facts in regard to impregnation after the menses have ceased and the change of life has been concluded are equally authentic and definite. It is not usual for such an event to occur, but it does occur occasionally. It is believed that the ovaries continue their functional activity

from the beginning till the end of life, and in not a few instances pregnancy has taken place many years after it was supposed the child-bearing function had ended. I am personally familiar with cases in which this interval has been ten to fifteen years, women from fifty to fifty-five years of age giving birth to healthy children.

TREATMENT.—It must be remembered in considering the question of treatment during this episode in a woman's existence that we are dealing with a situation which is common to all women who reach the limit of the child-bearing period though, of course, it is a situation which is by no means identical in all women.

It is not a disease, though disease frequently coexists with the change of life. It is a physiological experience which is often attended with morbid symptoms. The treatment of the coexisting diseases does not differ materially from that which would be proper if the change of life were not associated with them.

Diseases of the heart, liver, kidneys, brain, skin, blood-vessels, etc., are to be treated as such while the symptoms which mark the presence of the change of life have indications of their own, modified sometimes, it is true, by these diseases.

It seems hardly necessary to say that when no symptoms are present there is no occasion for administering treatment of any kind, any more than there would be at any other time in life.

With vast numbers of women the only symptom of which they are conscious is that their monthly sickness has become irregular in its occurrence, or has ceased altogether. With the majority of women there is no such thing as a crisis or a critical period at this time. Inasmuch, however, as this experience marks an epoch in life correlative, to a certain extent, with puberty it would not be wise, in any case, to ignore it.

With so many women it is a period of unstable equilibrium that it can do no harm to recommend universal caution and watchfulness during its continuance.

Diet.—Particular care should be exercised in selecting a simple but nutritious diet, and those who have been in the habit of indulging in the pleasures of the table must curtail them, avoiding food which is highly seasoned, avoiding fats and grease, avoiding an excess of meat, and using a minimum of alcohol, if any. Late suppers must be abstained from and all dietetic irregularities which demand unusual work from the digestive machinery.

Sleep.—Sleep is as essential as food at this time and in some instances is more essential. Particularly is this the case with hard-working women, with women of fashion, and with those who are neurasthenic, neurotic, and hypersensitive. If it is possible to get eight hours of sleep every night and one hour every afternoon, this will have a great influence in making the change of life an uneventful experience.

Air and Exercise.—Plenty of fresh air always, and exercise out of doors as much as possible are also important essentials and the contrast between those who follow such a course, whether from necessity or choice, with those who live indoors and are habitually deprived of a proper allowance of oxygen is often noteworthy enough, especially in the phenomena which are connected with the nervous system.

Clothing.—It seems superfluous to sound a note of caution in regard to clothing and yet the mode of dressing at the present time is notoriously provocative of diseases to which those who are going through the changes of life are particularly sensitive. The exposure of the neck and chest in the street, the exposure of the arms and body in evening costume, the insufficiency of skirts in street clothing, the unnatural shape of the shoes, these and other freaks of fashion are not only grotesque and inartistic, but are so unhygienic that the results of wearing them cannot help being injurious.

It is no wonder that the chilling of bodies thus exposed in winter, should result in congestions of the respiratory, digestive, and pelvic organs, and not infrequently in consequences which are serious. It is extremely important that the clothing of those who are going through the change of life should not only fit the body easily but should protect it sufficiently from changes in temperature, and this applies to every article with which the body may be covered.

Bathing.—Bathing is a most useful means of treatment in this condition, particularly for those who are anemic or debilitated or depressed, and it is unnecessary to take a long and expensive journey to a fashionable resort, in this country or in Europe, in order to obtain its beneficent influence.

In general it may be stated that warm baths are advisable, and cold baths inadvisable.

Sea baths are especially stimulating and helpful but not in water which is either very cold or very rough. Carbonic acid baths and salt baths may be taken at one's home, under proper directions, with great advantage.

Massage.—Systematic massage and passive exercise with Zander and other forms of mechanical apparatus, are also indicated for the weak and debilitated, for those who suffer with constipation, and for those who are neurasthenic and rheumatic.

Hot Flushes.—The most annoying, the most prevalent, and the most persistent of all the symptoms of the change of life are the hot flushes or hot flashes, the vasomotor storms, the sudden loss of control of the blood-vessels on the part of the vasomotor apparatus. They are emphasized by capillary engorgement and heat of the surface of the body and are usually followed by perspiration, and often by a copious flow of colorless urine. To relieve this symptom permanently and effectively requires the constant use of drugs and the symptom is not serious enough to warrant it. If the attacks are frequent an occasional dose of asafetida (10 grains), of bromide of sodium (20 grains), or of the tincture of valerian or of scutellarium will be useful as a sedative, and will certainly be preferable to the narcotic drugs which are too often given unnecessarily and form the basis of pernicious habits.

Headache.—With the hot flashes there is frequently an accompanying headache and this may be relieved by one of the above mentioned drugs supplemented, if necessary by a combination of caffeine (1 grain), camphor (2 grains), and acetanilide (5 grains).

This combination has usually been very satisfactory in the writer's experience.

Constipation.—The obstinate constipation which is so common a symptom of the change of life can usually be relieved by the fluidextract of cascara, or the well-known pill of aloin, strychnine, and belladonna better than by the more powerful cathartics. The writer has found these agents preferable to the salines, except possibly the sulphate and the phosphate of sodium, unless the case is one in which there is pelvic congestion and it becomes desirable to unload the vessels by means of copious watery discharges from the bowel.

Pelvic Congestion.—The pelvic and other congestions may also be relieved by the direct abstraction of blood from the cervix uteri. This may be done by means of leeches, by punctures with a scalpel, or by a Bier cupping-glass. This form of depletion is particularly desirable when the congestion is accompanied with sexual desire which is often a very annoying symptom to very worthy women.

Anemia.—Many women suffer with anemia at this time, either as the result of profuse bleeding from the uterus or from other causes. The bleeding must be checked by hot and astringent vaginal douches,

rarely by uterine douches, by tampon of the vagina or uterus, by application to the endometrium of ergot, hydrastis, antipyrine, iron, iodine, alum, etc., or by curettage if other means have failed. If the bleedings are too persistent it may be necessary to remove the uterus and this is especially the case if the curettage indicates that malignant disease is developing.

Worry.—Those who experience discomfort and misery during the change of life are also the women who worry, who are troubled with social and domestic cares, and who suffer from poverty, disappointment, and sorrow. Furthermore they are the women who have led irregular or dissipated lives, and who have suffered more or less from disease, particularly from disease of the pelvic organs. Of course the effective removal of all these unfavorable conditions is not always possible. In so far as they can be removed before the advent of the change of life, to that extent will the result be favorable. when that event occurs.

Internal Treatment.—For internal treatment tonics, quinine and strychnine, are useful and also some approved preparation of organic iron. There are of course many women who imagine that they are sick when passing through this experience, but who are not, so far as careful observation can determine.

It is of no use to ridicule such women, it is of no use to fill them with drugs. They should receive kind but firm treatment, be encouraged to cultivate self-control and to devote themselves to some absorbing occupation on behalf of others. A women who is thoroughly and unselfishly occupied does not have time to conjure up imaginary ills.

ANDREW F. CURRIER.

Channel Islands.—The Channel Islands, comprising Jersey, Guernsey, Alderney, Sark, and several smaller rocky islets, are situated in the bay of St. Michael, off the coast of Normandy, and lie between the latitude of 49° 10′ and 49° 42′ North and 2° 2′ and 2° 40′ West longitude. Guernsey and Jersey are the only two islands which require consideration as health resorts, and their claim as such is based upon the mild sunshiny nature of their climate, especially in the late autumn and winter. "Recent statistics show that Jersey receives more sunshine than any other part of the United Kingdom." In these island "camellias and rhododendrons flower in the open in February, frost is rare and lasting snow unknown." St. Helier's in Jersey and St. Peter's Port in Guernsey are the chief towns. The following table gives the climatic characteristics of Guernsey, which are practically the same as those for Jersey.

CLIMATE OF GUERNSEY AND JERSEY. MEANS FOR TEN YEARS. HEIGHT ABOVE MEAN SEA-LEVEL, 180 FEET.

	January to March.	April to June	July to September.	October to December.	Year.
Temperature—					
Mean average.....	43.7° F.	53.0° F.	60.5° F.	48.8° F.	51.5° F
Mean daily range...	7.6	10.8	10.9	7.6	9.2
Mean of warmest...	47.5	58.4	66.0	52.6	56.1
Mean of coldest.....	39.9	47.6	55.1	45.0	46.9
Mean rel humidity.	87%	83%	83%	86%	85%
Precipitations—					
Average in inches...	7.53	5.82	6.96	12.22	32.53
Wind—					
Prevailing direction	.....	.....	.....	.....	W. and S. W.
Weather—					
Amount of sunshine.	304 hrs.	665 hrs.	648 hrs.	247 hrs.	1864 hrs
Mean cloud	7.1%	6.0%	6.6%	7.2%	6.6%
Rainy days.....	47	34	39	59	179

From this table we see that the general climate of these two islands (Jersey and Guernsey) is a mild, moist, marine one. The diurnal range of temperature is small, and there is an average of five hours of daily sunshine. Of the total rainfall one-fourth occurs in the months of October and January. March and April are considered the most trying time of the year on account of the northeasterly winds.

Of course the islands are exposed to the winds from all directions, which, coming from the ocean, are moist and salt-laden. The prevailing winds are westerly and southwesterly, especially the latter.

The following table of yearly averages of wind is given for Guernsey, for the period from 1845 to 1862, inclusive:

Northeast wind prevailed on 100 days.
Southwest wind prevailed on 104 days.
Northwest wind prevailed on 110 days.
Southeast wind prevailed on 51 days.

The drinking water is obtained, for the most part, from wells. The drainage at St. Helier's and St. Peter's Port is by sewers into the sea.

The therapeutic effects of this climate arise from its mild sunshiny nature and its marine atmosphere. Elderly persons with low vitality and those with bronchial affections derive benefit from it. It is also of especial value for delicate scrofulous children and those of rachitic tendencies. It is unfavorable, on account of its moisture, for rheumatism, neuralgia, and renal diseases. Those with a tendency to respiratory troubles should not remain after the end of February. The Channel Islands are reached by boat from Southampton, Weymouth, or Plymouth in from six to ten hours, or from St. Malo or Granville, France, in two or three hours.

From a personal visit to Jersey the writer can testify to the delightful scenery of the island, both land and water, and the charm of the lovely drives through the winding roads, bordered by luxuriant vegetation. The air is fresh and invigorating and the sunshine most brilliant.

The writer desires to express his indebtedness in the preparation of this account of Guernsey and Jersey to "The Climates and Baths of Great Britain," by the Royal Medical and Chirurgical Society of London, 1895.

EDWARD O. OTIS.

Charcoal.—See *Carbo.*

Charcot, Jean Martin.—Born in Paris, France, on November 29, 1825. It is said that, even as a lad, he showed a strong leaning toward two vocations, viz , that of an artist (a painter. more particularly) and that of a physician. Finally, however, he decided in favor of a medical career. He received his degree of Doctor of Medicine in 1853. In 1862 he became connected with the department for women's diseases in the Salpêtrière Hospital, in Paris, and from 1866 to 1878 he delivered in that institution regularly, every year, lectures on chronic diseases, on diseases of old age, and especially on diseases of the nervous system. It was particularly the lectures on the latter diseases which made his name so famous. In 1872 he was made Professor of Pathological Anatomy in the Medical Faculty of Paris. Finally, the French Government decided, in recognition of the valuable work which he was doing in nerve-pathology, to establish at the Salpêtrière a new Clinical Chair of Nervous Diseases and to confer it upon Charcot. He accepted this professorship and continued to perform its duties up to the time of his death on August 18, 1893.

Both as a lecturer and as an original investigator Charcot's career was extraordinarily successful. His scientific contributions to medical literature are very numerous and cover a wide extent of terri-

tory. The shorter ones are to be found in the three periodicals which he aided in establishing and also in editing, viz., the "Archives de physiologie normale et pathologique" (from 1868 onward); the "Archives de neurologie" (from 1880 onward); and the "Revue Mensuelle de médecine et de chirurgie" (first established under this title in 1877, and then in 1878 given the title of "Revue de médecine"). In the domain of nervous diseases he published two larger treatises of first-class importance, viz., "Leçons

Fig. 1351.—Jean Martin Charcot.

sur les maladies du système nerveux faites à la Salpêtrière," Paris, fourth edition, 1880 (it has also been translated into many foreign languages); and "Localisations dans les maladies du cerveau et de la moelle épinière," Paris, 1876–1880. The latter work was awarded the Monthyon Prize in 1880. Pagel, from whose "Biographisches Lexikon" the data for this notice have been obtained, speaks of Charcot as one of the "grandes gloires de la nation française."

A. H. B.

Charleston Artesian Wells.—Charleston County, South Carolina.

Post-office.—Charleston.

Several artesian wells in the city of Charleston have been found to be impregnated with mineral ingredients. Those mentioned in the Geological Reports are the "Old Artesian Well," the "Citadel Green Well," the "Commercial Cotton Press Well," and "Chisholm's Mill Well." The following is an analysis of the first of these, made in 1868 by Dr. C. U. Shepherd, Jr.:

Old Artesian Well.

One United States Gallon Contains:

Solids.	Grains.
Sodium bicarbonate	71.06
Calcium bicarbonate	.12
Magnesium bicarbonate	.02
Sodium chloride	63.38
Silica	Trace.
Organic matter	Trace.
Iron oxide	Trace.
Aluminum oxide	.79
Carbonic acid	Trace.
	135.37

This water has a temperature of 87° F., and is therefore a thermal. The well is 1,250 feet deep, and the flow of water is estimated at 1,200 gallons per hour. The Commercial Cotton Press Well contains a considerable proportion of sulphate of magnesium. The two old wells on the corner of Wentworth and Meeting streets are owned by the city and are known as the Public Artesian Wells. One is 1,180 feet deep, the other is 1,240 feet deep. There are also two 2,000 foot wells, one located on Marion Square and owned by the city; the other on George Street and owned by the Charleston Water Works Company. The water from the latter two wells is better and more palatable than that from the Public Artesian Wells.

Emma E. Walker.

Charleston, S. C. A city of 58,833 inhabitants and one of the chief seaports of the south, situated upon a point of land between the mouths of the Ashley and Cooper rivers, several miles from the Atlantic Ocean. It is an attractive old-fashioned town, with rich vegetation of a more or less semitropical nature. It is a convenient and interesting place to spend some time in, on one's way north from the more Southern resorts, especially in the spring. The magnolia gardens in the vicinity are most interesting and well worthy of a visit. Indeed, both by water and land the excursions are many and attractive. The writer recalls very vividly the delight of a visit here in the spring when returning from Florida. The mild balmy atmosphere, the profusion of roses, the jasmine, the strawberries, the quaint and attractive streets and residences, and the numerous excursions, were a constant source of pleasure.

As will be seen from the climatic table, the winter and spring climate is a mild, equable, marine one. The proximity of the sea renders the relative humidity greater than at the resorts farther inland; hence this is not a favorable climate for a permanent residence for the consumptive.

Climate of Charleston, S. C. Latitude, 32° 47′; Longitude 79° 56′. Period of Observation, 12 Years 10 Months.

Data.	January.	March.	July.	November.	Year.
Temperature (Fahr.)—					
Average or normal	49.5°	57.8°	82.8°	57.2°	65.9°
Average daily range	14.6	15	14.1	14.1	
Mean of warmest	58.4	67.1	90.2	65	
Mean of coldest	43.8	52.1	76.1	50.9	
Highest or maximum	80	85	104	82	
Lowest or minimum	23	28	67	28	
Humidity—					
Average relative	75.4%	69.6%	74.3%	74.7%	73.8%
Precipitation—					
Average in inches	3.77	4.47	7.18	3.51	59.9
Wind—					
Prevailing direction	N.	S.W.	S.W.	N.E.	S.W.
Average hourly velocity in miles.	7.3	8.8	7.7	7.5	7.9
Weather—					
Average number of clear days.	9.5	12.7	10.4	11.5	134
Average number of fair days.	10.5	10.8	14.6	10.5	140.3
Average number of clear and fair days.	20	23.5	25	22	274.3

Edward O. Otis.

Chartæ.—*Papers.* Sheets or strips or variously shaped pieces of absorbent paper impregnated with medicinal substances. There is one official charta, and two others are contained in the National Formulary.

		Composition.
Charta Sinapis (Mustard paper).	U. S. P.	Black mustard 100, rubber 10, petroleum, benzin, and carbon disulphide, q.s. To be dipped in warm water and applied to the skin as a rubefacient.
Charta Cantharidis (Cantharides paper).	N. F.	White wax 80, spermaceti 30, olive oil 40, Canada turpentine 10, cantharides 10, water 100. Employed as a rubefacient or vesicant.
Charta Potassii Nitratis (Potassium nitrate paper).	N. F.	Potassium nitrate 20, distilled water 80. Blotting paper is dipped in this solution, and then dried. It is burned and the fumes are inhaled for the relief of asthma.

R. J. E. Scott.

Chassaignac, Charles Marie Édouard.—Born in Nantes, in the western part of France, on December 22, 1804. He received the degree of Doctor of Medicine from the University of Paris in 1835. The name of Chassaignac is known to the medical world as that of the man who introduced two important surgical procedures to the knowledge of the profession, viz., the use of a strong steel-chain snare for crushing through the pedicle of a tumor ("Traité de l'écrasement linéaire, etc.," Paris, 1856), and a method of effectively draining a suppurating wound ("Traité pratique de la suppuration et du drainage chirurgical," two volumes, Paris, 1859). He is also entitled to credit for certain improvements which he made in the operation of tracheotomy ("Leçons sur la trachéotomie," Paris, 1855), and for having written a very useful work on clinical surgery ("Traité clinique et pratique des opérations chirurgicales, etc.," two volumes, Paris, 1861 and 1862). He died at Versailles on August 26, 1879. A. H. B.

Chattanooga, Tenn.—A city of about 45,000 inhabitants, situated in the southeastern portion of Tennessee, upon the Tennessee River. It is 762 feet above sea level, and the surrounding mountains are from 1,320 feet—Missionary Ridge—to 2,160 feet—Lookout Mountain—both of which points are easy of access. The scenery is varied and beautiful, and the atmosphere is exhilarating and pure. The spring is early, opening in March, and the vegetation rich and varied. The soil is dry and loamy, and the drainage good. There are occasional winds and fogs, but the city is so surrounded by mountains that it is greatly shielded in this way from the winds. The climate is indicated in the accompanying table, kindly obtained for the writer by Dr. W. A. Applegate of Chattanooga. From this it is seen that the winter climate is moderate and the summer not excessively hot. The relative humidity is quite high, and the average number of clear and fair days not remarkably large in comparison with other health resorts in the South. The daily range of temperature is also seen to be large.

Judged from its climatic conditions solely, Chattanooga would hardly fall within the list of genuine health resorts, although, like so many partisan reports upon health resorts, its "climate conditions" are vaunted as "unsurpassed by any point in this country." It is needless to say that the writer who makes this statement gives neither full climatic tables nor any series of results obtained in the treatment of disease. Undoubtedly a residence in some of the high localities about the city offers, in the pure and bracing atmosphere, mild winter temperature, and attractive scenery, substantial climatic advantages in the treatment of pulmonary tuberculosis; for the chief end of all climatic treatment of consumption can well be accomplished here, namely, constant exposure to pure outdoor air. A sanatorium, for instance, on Lookout Mountain, conducted as Falkenstein or the Adirondack Cottage Sanitorium is, would doubtless exhibit equally good, if not better, results. Formerly malaria was very prevalent here, but since the sanitary condition of the city has been improved, this disease is said to have disappeared to a very great extent.

Chattanooga, Tenn. Latitude, 35° 4′; Longitude, 85° 15′. Climatic Data from Observations from 1879 to 1899 Inclusive.

	January.	February.	March.	April	May.	June.	July.	August.	September	October	November.	December.	Year.
Temperature Fahr.—													
Average or normal	41.4°	45.4°	51.1°	61.0	68.5°	75.9°	78.4°	77.0°	71.8°	61.6°	50.3°	43.7°	59.9°
Average daily range	16	17.4	18.7	20.1	20.8	19.8	18.4	18	19.2	20.1	18.5	17.1	19.3
Mean of warmest	52.2	54.0	56.6	65.0	71.8	78.9	81.1	80.8	75.8	67.2	55.8	57.2	66.3
Mean of coldest	33.6	33.8	45.7	55.4	65.4	72.2	75.4	73.8	68.1	56.5	45.4	38.1	55.3
Highest or maximum	75	78	85	90	93	98	101	100	98	91	79	73	88.4
Lowest or minimum	2	−2	15	25	40	45	56	54	38	27	16	3	26.9
Humidity—													
Average relative	76%	71%	67%	64%	69%	73%	75%	77%	76%	74%	71%	74%	74.2%
Precipitation—													
Average in inches	6.19	5.32	5.95	4.52	3.89	4.49	4.22	3.80	3.70	2.71	3.71	4.31	52.81
Wind—													
Prevailing direction	N. E.	N. W.	N. W.	S.	S. W.	S. W.	S. W.	N. E.	N. E.	N. E.	S.	S.	
Average hourly velocity in miles	6.9	7.5	7.7	7.1	5.5	4.9	4.8	4.6	4.6	5.2	6.1	6.6	5.9
Weather—													
Average number of clear days	7	7	9	11	10	9	8	9	12	15	11	8	116
Largest number of clear days	12	13	18	18	19	16	16	15	21	23	22	14	207
Smallest number of clear days	2	3	4	5	2	4	2	5	5	8	6	1	47
Average number of fair days	11	10	11	12	15	15	16	15	12	10	9	11	147
Largest number of fair days	17	17	15	18	23	19	22	19	18	15	14	15	212
Smallest number of fair days	4	6	5	6	7	11	8	10	6	4	5	6	78
Average number of cloudy days	13	11	11	8	6	6	7	7	6	6	9	12	102
Largest number of cloudy days	22	16	17	14	13	15	13	13	12	13	15	17	180
Smallest number of cloudy days	7	8	4	3	1	1	1	3	0	3	3	8	42
Average number of rainy days	14	12	13	11	11	12	14	12	9	8	9	11	136
Smallest number of rainy days	9	6	7	6	5	6	6	5	2	3	3	5	63
Largest number of rainy days	24	22	21	17	16	19	19	18	16	13	19	17	221

The outdoor attractions are many and varied; excursions to the various battlefields—Chickamauga, Missionary Ridge, Lookout Mountain, and Orchard Knob—are all full of interest. The view from Lookout Mountain, as the writer can testify from personal experience, is a striking one, looking down upon the winding river and the other lesser heights. The roads are good, and driving and wheeling are popular amusements.

The accommodations are excellent as regards both hotels and boarding-houses. "Lookout Inn" on Lookout Mountain is open all the year and affords the best of accommodations.

Chattanooga is a railroad center and is easily accessible from all directions. EDWARD O. OTIS.

Chauffeur's Fracture.—See *Automobile.*

Chaulmoogra.—*Chawul-Mungri.* The seeds of two species of *Gynocardia* (fam. *Flacourtiaceæ*) of Southeastern Asia; also the oil expressed from them and the bark, the latter not being an article of commerce with us. The seeds of commerce are commonly referred to *G. odorata* R. Br. This species, however, does not yield the ordinary seeds, which contain no prussic acid, but a different variety, rare in commerce and rich in prussic acid. The species yielding the commercial seeds appears undescribed, though it is indefinitely referred to by various authors. The bark employed is possibly that of the *G. odorata*, because prussic acid is developed in its infusion, which is also astringent, hence much like wild-cherry bark. It is used as a febrifuge. The fruit pulp is used to poison fish. The seeds and the oil expressed from them are extensively employed, externally and internally, in the East, as a remedy for leprosy and for various skin diseases.

The plant is a tree, and bears directly from its trunk and large branches, globoidal berries, as large as a shaddock, containing numerous seeds. The latter are about one inch or one inch and a quarter long, irregularly ovoid, angular from pressure, and dull gray. The kernel shrinks away from the testa in drying, the latter being thin and brittle. The oily kernel, at first white, becomes brown. It has a disagreeable odor and taste. The seeds consist of about half their weight of a brownish-yellow fixed oil, of a specific gravity of about 0.945. The active portion of this oil appears to be its twelve per cent. of gynocardic acid, with two of cocinic, four of hypogeic, and sixty of palmitic acids. The oil has been considerably employed in professional practice, both externally and internally, in skin diseases. The dose is ♏ iij.–iv. (0.2–0.25) after meals, gradually increased. Doses of ♏ x. (0.6) have been found irritating to most persons, resulting in vomiting and purging.

Gynocardic acid has also been employed and is said not to cause nausea. An ointment made of fifteen to twenty-five grains of this acid to the ounce of vaseline has been recommended as an application to dry patches of eczema.

False chaulmoogra is the seed of *Hydnocarpus anthelmintica* Pierre, a related plant. It is similarly used in native practice, and also as an anthelmintic.

HENRY H. RUSBY.

Cheese Mites.—Mites of the family *Troglyphinæ*, minute forms with a soft body, without eyes or tracheal respiratory tubes. They live in such dry or decaying materials as flour, sugar, cheese, and prunes. Their small size makes their introduction on or into the human body easy, and they have been reported from the alimentary canal and skin. See *Arachnida.*

A. S. P.

Cheilitis Glandularis Apostemose.—See *Myxadenitis Labialis.*

Chelidonium.—*Garden Celandine.* The entire plant, *Chelidonium majus* L. (fam. *Papaveraceæ*). In some pharmaco pœias the root only is recognized, but the composition and properties are the same throughout. This, the only species of the genus, is a perennial herb, with slender branching stem, bright yellow delicate flowers, and an acrid, irritating, disagreeable-smelling yellow juice. Root several-headed, branching, red-brown; stem about twenty inches (50 cm.) long, light green, hairy; leaves about six inches (15 cm.) long, petiolate, the upper ones smaller and sessile, light green, on the lower side glaucous, lyrate-pinnatifid, the pinnæ ovate-oblong, obtuse, coarsely crenate or incised and the terminal one often three-lobed; flowers in small, long-peduncled umbels with two sepals and four yellow petals. Capsule linear, two-valved and many-seeded. The fresh plant contains a saffron-colored milk-juice and has an unpleasant odor and acrid taste.

FIG. 1352.—Celandine, slightly reduced. Seed enlarged about four times. (Baillon.)

Celandine is a native of Europe, but has been abundantly naturalized in the United States, where it affects rich, shaded dooryards. It is an old country medicine, and has been used to dissipate warts and as a dressing for ulcers. Its general composition is very similar to that of bloodroot, but the important alkaloid is *chelerythrine*, associated with *chelidonine*, *α* and *β homochelidonines* and *protopine.* There are also *chelidonic* and *chelidoninic acids.* Chelerythrine acts in a markedly different way from its close relative, sanguinarine, lacking entirely the irritating properties of the latter upon the motor centers, which it depresses or paralyzes from the first. It also depresses the muscles. The ends of the sensory nerves are first irritated and then depressed. Chelidonine tends to counteract this primary sensory stimulation. The homochelidonines and protopine are in very small amounts. Their effects are also in the general direction of both sensory and motor depression. Hence the effects of celandine are not violently irritating like those of bloodroot, and are finally soothing and depressing. There is, however, enough sanguinarine, in connection with the primary sensory irritation of the chelerythrine, to make the drug strongly irritating in the first stage of action. It acts as a laxative or a purgative, and has always been regarded as an active cholagogue. Large doses may cause emesis, but the tendency of this drug is purgative, as that of sanguinarine is emetic. There is no official preparation. The dose is gr. xv. to lx. (1.0–4.0). The extract is mostly used, in doses of gr. viij. to xv. (0.5–1.0). The drug has been a favorite domestic basis for poultices, and the juice is a counterirritant, similar to bloodroot.

HENRY H. RUSBY.

Cheloid.—See *Keloid.*

Chelytus.—A genus of mites sometimes found among old books or rags, but more commonly in stables,

poultry houses, old feed bins or tobacco store-houses, and tombs. Its members, though predacious, have not been known to attack man, but they are often found on his body. See *Arachnida*. A. S. P.

Chemistry, Physiological.—Physiological chemistry may be defined as the chemical branch of physiology. It is concerned with the chemistry of substances, processes, and conditions relating to normal organisms. For this purpose the facilities offered by physical chemistry, inorganic chemistry, and organic chemistry are utilized. Physiological chemistry is therefore fundamentally chemical in its methods and essentially physiological in its purposes. In accordance with this idea the physiological chemist seeks to explain physiological phenomena by chemical methods.

The character of the substances that must engage the attention of the physiological chemist is exceedingly diverse, varying from the simplest types of chemical compounds to those of extreme complexity. Equally variable are the physiological processes and conditions for which the science under discussion is endeavoring to offer an explanation.

In a general way the chief object of physiological chemistry is a complete understanding of the principles of normal nutrition in its broadest sense, that is, a complete knowledge of the laws underlying all the processes concerned in the normal metabolism of living organisms and especially those relating to man. Nutrition is essentially chemical in nature and therefore in the solution of the problems concerned chemical methods are imperative.

It is difficult to make a sharp division between physiologial chemistry and the sister science, pathological chemistry, since physiology and pathology are almost inseparable. In many instances pathological conditions and processes are utilized by the physiological chemist for the explanation of normal nutrition. From the foregoing definitions it is apparent that physiological chemistry is of exceeding great importance in its relation to physiology, pathology, and the practice of medicine. The importance of physiological chemistry to the medical sciences may be inferred from the position which it has assumed in the curricula of the medical schools, for every institution deserving the designation of medical school to-day offers courses of varying merit in this subject. In the best courses offered the student makes a thorough study of the chemical composition of the food-stuffs and of the various tissues and fluids of the body. The chemical and physiological processes of digestion, absorption, secretion, excretion, and nutrition in general are considered together with the application of analytical methods to the problems of metabolism and to the identification and estimation of biological products.

The science of physiological chemistry is comparatively young since prior to the year 1800 practically little had been accomplished from a strictly physiological chemical standpoint. With the old medical chemistry of the so-called iatro-school it has nothing in common and in no way is it to be regarded as a development of that science. It is true that previous to the date given above certain contributions had been made concerning the chemistry of vegetable and animal substances but no rational theory of chemical combination had been evolved to make the isolated facts of real value. Previous to the discovery of oxygen by Priestley and Scheele and to the time of the accurate weighings and measurements of Lavoisier and his antiphlogistic theory very little resulted from the investigations that had been carried on for hundreds of years by able physicians who zealously interested themselves in the chemistry of the human body and its processes. However, from out the mass of early investigators the names of van Helmont, de Graaf, Boerhaave, Réaumur, Stevens, Mayow, and Spallanzani are especially worthy of mention since they are intimately associated with the beginnings of a clear understanding of the digestive processes and the nature of respiration. The discoveries of Lavoisier published in the latter part of the eighteenth century led to a clear conception of combustion as a process of oxidation. He further showed that the oxygen inspired through the lungs is used in the body for the oxidation of various compounds, carbon dioxide and water being among the decomposition products. The nature of animal heat was carefully considered and the rôle played therein by oxygen was demonstrated. In short the fundamental features of respiration were established and a clear trail was blazed for real scientific progress.

With the beginning of the nineteenth century discoveries of special importance to physiological chemistry were made. Thus Chevreuil's investigation of fatty bodies of animal origin; the work of Berzelius on urine and blood; that of Prevost and Dumas on the composition of the blood and urea formation; the researches of Tiedemann and Gmelin on the nature of digestion; and the determination of the correct formula of urea by Prout as early as 1819 may be cited as especially pertinent examples of investigation which have since become classic. Up to this time knowledge of the chemistry of organic compounds had remained far in the background of the rapidly increasing information concerning inorganic chemistry. For this reason very little progress had been made in physiology. The turning point, however, was reached in 1828 when Wöhler accomplished the synthetic formation of urea from ammonium cyanate. Up to this time urea was known only as a product of animal processes. The possibility of the preparation of this organic compound from inorganic materials opened up an entirely new line of thought which has led to the present day position of organic chemistry, and has been of prime importance for the development of physiological chemistry. Wöhler's experiment will ever be memorable since it removed at a single blow the artificial barrier that had been raised between organic and inorganic chemistry.

During the early portion of the nineteenth century, important advances were made in other fields. Thus Kirchluff in 1814 found that germinating barley seeds contain a substance that can be extracted with water and which is capable of transforming starch into sugar. Later this active agent was isolated and given the name of diastase; in 1824 Prout, Tiedemann, and Gmelin, independently discovered the presence of hydrochloric acid in the stomach secretion; in 1825–33 William Beaumont conducted his classic experiments on Alexis St. Martin; Leuchs discovered diastase in saliva in 1831; in 1834 Eberle prepared an artificial gastric juice; Schwann, in 1836, postulated the existence of pepsin and made the first biliary fistula; three years later Wasmann isolated pepsin, and in 1842 Bassow and Blondot made a gastric fistula in the dog; Heinz found the milk-curdling enzyme in 1851 and in the same year Lehmann isolated lactic acid from gastric contents. Five years later Meissner investigated the products of gastric digestion of proteins and in 1872 Ebstein and Grützner postulated the existence of pepsinogen. At first the action of enzymes was compared to that found in alcoholic fermentation induced by yeast and to the processes concerned in putrefaction. It was Berzelius who first suggested that the digestive agents act by catalysis.

For ten years subsequent to the synthetic formation of urea by Wöhler inorganic and analytical chemistry were greatly extended, resulting in a better conception of chemical system and the improvement of analytic methods, much of which was due to the labors of Berzelius, the foremost chemist of the time. In the hands of Berzelius and Liebig these new methods

greatly increased the knowledge of organic chemistry. A great number of new organic compounds were prepared, but their mode of formation, their characteristics and their manner of decomposition more or less contradicted the theoretical conceptions which Berzelius sought to transfer from his system of inorganic chemistry over to the organic field. There now arose a thirty years' controversy on theoretical chemistry which was waged furiously between the leading chemists, but it proved fruitful in investigation, especially in organic chemistry. "Organic synthesis, together with the explanation of theoretical points; the rearrangement of groups on physical and chemical grounds; the mechanical theory of gases and vapors, which first gave a foundation for the estimation of the relative weight of molecules and the number of atoms contained therein; the relation of atoms in molecules; and the theory of organic chemistry in its essentials, founded on the affinities of the carbon atoms—offering many points difficult of solution and still controverted—all was the fruit of this period." The progress during this period was due in large measure to the work of Laurent and Kekulé, although it would be difficult to enumerate all the chemists who are entitled to a share of the credit

By 1864 the controversy had somewhat abated but in the meantime physiological chemistry had almost been overlooked save for the work of Justus von Liebig (1803–1873) who may be regarded as the father of physiological chemistry. For forty years he labored to advance it and many of the views formulated by him are accepted at the present time although perhaps somewhat modified. Among his more important contributions to physiological chemistry may be cited the theory of the origin of animal heat. It was he who developed the idea that the sensible heat of the body may be explained by processes of combustion accomplished within the organism. From investigation of the source of animal heat Liebig was led to a consideration of the nature of food itself and he classified foods according to the functions they were assumed to perform in the organism. "The food of man and animals," he says, "consists of two classes of substances essentially different in their composition. The one class (consisting of nitrogenous substances, albumin, etc.) serves in the formation of blood and building up the various organs of the body; it is called plastic food. The other (consisting of non-nitrogenous substances, the fatty bodies, and the so-called carbohydrates) resembles ordinary fuel serving, as it does, in the generation of heat; it is designated by the term respiratory food. Sugar, starch, and gum may be looked upon as woody fiber, from which, it is known, they are capable of being formed. Fat, by the quantity of carbon it contains, stands nearest to coal. We heat our body exactly as we heat a stove, with fuel which, containing the same elements as wood and coal, differs essentially, however, from the latter substances by being soluble in the juices of the body." While this classification of foods is not entirely acceptable to-day it served as a sure foundation upon which has been built the imposing superstructure of our present knowledge concerning food-stuffs. From his study of the foods we are also indebted to Liebig for his theory of animal nutrition. "According to this theory, the plant holds a position intermediate between the mineral and animal world. The animal is incapable of assimilating the compounds stored up in inorganic nature. To render these compounds subservient to the purposes of animal life they may have to undergo a preliminary preparation within the living organism of the plant. The simple mineral molecules are thus converted into molecules of a higher order, fit to serve in building up and maintaining alive the body of the animal. In his "Familiar Letters on Chemistry," he says, "How admirably simple after we have acquired a knowledge of this relation between plants and animals, appears to us the process of formation of the animal body, the origin of its blood and of its organs! The vegetable substances, which serve for the production of blood, contain already the chief constituent of blood ready formed, with all its elements. The nutritive power of vegetable food is directly proportional to the amount of these consanguineous compounds in it; and in consuming such food, the herbivorous animal receives the very same substances which, in flesh, support the life of carnivora." "From carbonic acid, water, and ammonia, that is, from the constituents of the atmosphere, with the addition of sulphur and of certain constituents of the crust of the earth, plants produce the blood of animals; for the carnivora consume, in the blood and flesh of the herbivora, strictly speaking, only the vegetable substances on which the latter have fed."

"A comprehensive natural law connects the development of the organs of an animal, their growth and increase in bulk, with the reception of certain substances essentially identical with the chief constituents of its blood." "The animal body is a higher organism, the development of which begins with these substances, with the production of which the life of those vegetables which are commonly used for food ends. The various kinds of grain and of plants used for fodder, die as soon as they have produced seeds. In the infinite series of organic products which begins with the inorganic food of plants, and extends to the most complex constituents of the nervous system and brain of animals the highest in the scale, we see no blank, no interruption. The nutritive part of the food of animals, that from which the chief material of their blood is formed, is the last product of the productive energy of vegetables."

No account of Liebig's achievements in the domain of physiological chemistry is complete without reference to his doctrine of the origin and function of fat in the organism. This type of question had never been duly considered previously. As a result of a careful series of investigations he was led to the conclusion that fat formation takes place within the organism and the materials concerned in fat formation are the carbohydrates which the animal finds stored in plant tissue ready for use. Dumas and Boussingault in France were especially antagonistic to this view, their idea being that fat is merely transferred from the plant to the animal. Needless to say Liebig's view was later confirmed and is accepted at present. In other directions than those recorded above, Liebig's work was extensive. His examination of the blood and bile; his researches on the chemical composition of the urine of man and of the carnivora; his study of the relation of the reaction of urine and the nature of the food consumed, leading finally to the elaboration of a method for urea estimation; and the classic investigation of uric acid in company with Wöhler may be cited as examples. Previous to the time of Liebig little was known concerning the nature of the juice, or extract, of meat. Chevreuil, twenty years previously, had indicated the existence in it of a substance called creatine. Liebig formulated the structure of this compound of which even the chemical composition was unknown. He studied its decomposition products, creatinine and sarcosine, as well as many other compounds that play a very significant rôle in the animal economy. At the same time his investigations on meat extract opened up a vein in organic chemistry the depth of which has not yet been reached. It must also be remembered that it is to Liebig that science is indebted for the discovery of chloroform and chloral. In cooperation with Wöhler glucosides were discovered, and their recognition of the influence of enzymes upon glucosides was an important contribution to the knowledge of enzymes.

The status of physiological chemistry in the time

of Leibig may best be expressed in his own words written in 1852. "After mineral chemistry had gradually attained its present state of development, the labors of chemists took a new direction. From the study of the constituent parts of vegetables and animals, new and altered views have arisen; and the present work (Animal Chemistry, or Organic Chemistry in its Applications to Physiology and Pathology) is an attempt to apply these views to physiology and pathology." "In earlier times the attempt has been made, and often with great success, to apply to the objects of the medical art the views derived from an acquaintance with chemical observations." "With all its discoveries modern chemistry has performed but slender services to physiology and pathology; and we cannot be deceived as to the cause of this failure, if we reflect that it was found impossible to trace any sort of relation between the observations made in inorganic chemistry, the knowledge of the characters of the elementary bodies and of such of their compounds as could be formed in the laboratory, on the one hand, and the living body, with the characters of its constituents, on the other."

"Physiology took no share in the advancement of chemistry, because for a long period she received from the latter science no assistance in her own development. This state of matters has entirely changed in the last five and twenty years."

"How clear are now to us the relations of the different articles of food to the objects which they serve in the body, since organic chemistry has applied to the investigation her *quantitative method* of research!" When a lean goose, weighing four pounds gains, in thirty-six days, during which it has been fed with twenty-four pounds of maize, five pounds in weight and yields three and one-half pounds of pure fat, this fat cannot have been contained in the food, ready formed, because maize does not contain the thousandth part of its weight of fat, or of any substance resembling fat. And when a certain number of bees, the weight of which is exactly known, being fed with pure honey, devoid of wax, yield one part of wax for every twenty parts of honey consumed, without any change being perceptible in their health or in their weight, it is impossible any longer to entertain doubt as to the formation of fat from sugar in the animal body."

"We must adopt the method which has led to the discovery of the origin of fat, in the investigation of the origin and alterations of the secretions, as well as in the study of all the other phenomena of the animal body."

"The imperfection of the method or system of research adopted by physiologists can alone explain the fact, that for the last fifty years they have established so few new and solid truths in regard to a more profound knowledge of the functions of the most important organs, of the spleen, of the liver, and of the numerous glands of the body; and the limited acquaintance of physiologists with the methods of research in chemistry will continue to be the chief impediment to the progress of physiology, as well as reproach which that science cannot escape."

"Before the time of Lavoisier, Scheele, and Priestley, chemistry was not more closely related to physics than she now is to physiology. At the present day chemistry is so fused, as it were, into physics, that it would be a difficult matter to draw the line between them distinctly. The connection between chemistry and physiology is the same, and in another half century it will be found impossible to separate them." (A prophecy which has been completely fulfilled.)

"In the hands of the physiologist, organic chemistry must become an intellectual instrument, by means of which he will be enabled to trace the causes of phenomena invisible to the bodily sight."

The progress in physiological chemical research during the life time of Liebig was tremendous and the outlook as defined by him one of great inspiration. On the other hand, looking backward to the year 1830, twenty years before Liebig's prophetic words were written we find the future of physiological chemistry rather limited if the words of Thomson may be accepted as indicative of the general opinion on the subjection under discussion. In his History of Chemistry, he says, "The only functions of the living body upon which chemistry is calculated to throw light, are the processes of digestion, assimilation, and secretion."

The measure of Liebig's success has been estimated by Bischoff in the following words. "However great and immortal may be the services of Aristotle, Galen, Vesalius, Harvey, Linnaeus, Haller, Cuvier, Charles Bell, J. Müller, and others to physiology; however greatly they and others may have enriched our knowledge in the province of organic nature, I can find no proof in the history of science that any single one of these has so influenced and altered the views and methods of physiology, and also consequently of medicine, by facts and methods, as Liebig. I regard Liebig as the one who has brought organic natural science into the pathway of exact investigation."

While Liebig in Germany was applying chemical principles to physiological processes Mulder in Holland was pursuing investigations of a somewhat similar but more restricted nature. Mulder's work consisted principally in attempts to determine the nature of proteirs and of such substances as gelatin and the keratins. He also pointed out the close similarity between the nitrogenous compounds found in plants and those which occur in the blood of animals.

Shortly after Liebig had begun his scientific career investigations of a chemical character were instituted in France by Claude Bernard (1813–1878). His writings are very voluminous and treat of a great variety of topics. Bernard's doctorate thesis was entitled "Du suc gastrique et de son rôle dans la nutrition." The results obtained in this investigation undoubtedly had a decided influence in the determination of the character of his future work. The main conclusion of the thesis was that cane sugar when injected intravenously promptly reappears in the urine. These results led him to make a study of the sugars and their behavior in the body, an investigation that culminated in the discovery of glycogen and the now famous researches concerning the functions of glycogen in the organism. It is perhaps needless to point out that he was partly actuated to study the sugars because of his great interest in the problems suggesetd by the pathological state diabetes; he was anxious to discover the cause of the excess of sugar in this condition and so perhaps be enabled to find a remedy for it.

When Bernard began his work knowledge of digestive processes other than those connected with the stomach was practically nil. Gastric digestion was assumed to be a sufficient preparation for the easy absorption of food products. It is true that bile was considered of significance in digestion but the function of the pancreas was unknown. The researches of Tiedemann and Gmelin contained "all that we know with certainty relative to the changes which the chyme undergoes in the intestine" and all that these authors have to suggest is the possibility "that the casein of the pancreatic secretion containing a large proportion of nitrogen yields a portion of this element to different ingredients of the alimentary substances which contain less nitrogen, so as to reduce itself to their standard in this respect, and to convert them into albumin." It is mainly to Bernard that we owe our knowledge of the action of pancreatic juice, although Valentin in 1844 demonstrated that juice expressed from the pancreatic gland has an action upon starch, and Eberle had suggested that

the pancreas is in some way concerned with fat digestion. It remained, however, for Bernard to reveal its three-fold activity. "He showed that it, on the one hand, emulsified, and on the other hand, split into fatty acids and glycerin, the neutral fats discharged from the stomach into the duodenum; he clearly proved that it had a powerful action on starch, converting it into sugar; and, lastly, he laid bare its remarkable action on protein matters. Pointing out that the bile precipitates the products of the gastric digestion of protein matters, and puts an end to peptic changes, he went on to show that the pancreatic juice acted subsequently as well on these precipitated matters as on those protein constituents of a meal which had escaped solution in the stomach." "It is, in fact, the pancreatic juice which has the special property of completely dissolving these two kinds of material, for the digestion of nitrogenous substances is far from being completed in the stomach, though this is the accepted view. Two acts, perfectly distinct, take place in the stomach and in the intestine, the one duly following the other. Gastric digestion is only a preparatory act." The study of internal secretion which has since proved so fruitful was initiated by Bernard in his investigations on the function of glycogen.

In the laboratories founded by Liebig and Bernard were trained a great many of the well-known investigators of the closely succeeding years and the large number of men who became interested in the problems of physiological chemistry accounts in great measure for the extremely rapid growth of the science. In the space allotted it will be impossible to more than briefly mention the work associated with some of the older of these men most of whom have passed away only within the last few years.

The successor of Claude Bernard in the Collège de France was Brown-Séquard (1817–1894) to whom science is indebted in a great degree for investigation of problems connected with internal secretion, the practical application of which by him in 1889 was the starting-point of organotherapy. In 1856 he demonstrated that the adrenals function by means of an internal section and from this point of view valuable contributions to science were made concerning the function of various other ductless glands, particularly the pituitary and the thyroids.

With the name of Max Pettenkofer (1818–1901) are associated the Pettenkofer test for bile salts and the famous Pettenkofer respiration chamber. Pettenkofer, a pupil of both Scherer and Liebig, early manifested an interest in the study of metabolism. Bischoff in Giessen began nutrition experiments upon dogs and later worked in Munich with Voit. These experiments aroused the interest of Pettenkofer and led to the construction of the respiration chamber named for him which is characterized by furnishing the experimental subject a current of fresh air within the calorimeter. This is significant, for Pettenkofer was later mainly instrumental in bringing about recognition of the science of hygiene especially from its experimental side. Pettenkofer's object in building a calorimeter was to obtain complete information concerning the sources of loss and gain to the body over a considerable period of time, the man or animal experimented upon being maintained under perfectly normal conditions. In previous experiments on nutrition and the influence of various diets upon the same, account had been taken only of the nitrogen entering and leaving the body, the carbon, hydrogen, and oxygen remaining undetermined. Thus knowledge of the relation of diet to the oxidation of material in the body was very imperfect. Through the investigations of Pettenkofer associated with Voit a far more complete insight was obtained into the part played in nutrition by the different constituents of the food, the effects of variations in the quantity of food ingested, and many other important questions of a similar character. The experiments of the Munich school of which Pettenkofer was the head form the chief basis of our present knowledge of dietetics. The presence of creatinine in the urine was one of the important discoveries of Pettenkofer.

In his work on nutrition Pettenkofer was associated from the beginning with his pupil Carl Voit (1831–1908) who had also studied with Liebig and Wöhler. The inspiration which Voit had caught from contact with Liebig, Wöhler, and Pettenkofer, and from the classic work of Bidder and Schmidt impelled him to a closer investigation of problems relative to nitrogenous metabolism. His work with Bischoff on the laws of nutrition of the carnivora remains a classic of metabolism studies. The present-day conceptions of the fundamental principles regulating protein metabolism were first distinctly described by Voit. Thus, the laws of nitrogenous metabolism and the theory that muscle work is done preferably at the expense of non-nitrogenous substances were first clearly elucidated by him. In the study of intermediary metabolism he was also a pioneer, since among his varied types of activity may be mentioned experiments designed to discover the significance in metabolism of such compounds as gelatin, proteoses, peptone, asparagin, etc.

While Voit was enunciating the principles of nitrogenous metabolism at Munich Edward Pflüger (1829–1910) at Bonn was rendering to physiological chemistry an incalculable debt by his criticisms of theories promulgated by physiological chemical investigators. His controversies with Voit on nitrogenous metabolism in particular did much to put the subject upon a basis better grounded than otherwise might have been possible. The theory of Pflüger on nitrogenous metabolism never received the support accorded to the rival theory of Voit although it contains some ideas of considerable strength. While Pflüger's name is closely associated with nitrogenous metabolism the real constructive contributions offered by him were those concerning the principles of glycogen formation. In spite of the fact that his scientific life was one of great activity and the number of papers published by him was very large, perhaps his greatest influence upon the development of physiological chemistry has been to subject to criticism the work of others and in a sense sift the wheat from the chaff. His motto "Die Kritik ist das wichtigste Motiv jeden Forschrittes, deshalb übe ich sie" (Criticism is the most important motive in progress of any sort, therefore I practise it) shows his peculiar type of mind. To him also belongs the credit for the establishment of the eminently successful *Archiv für die gesamte Physiologie*, known as Pflüger's Archiv, the purpose of which was to publish articles in any way related to physiology.

The name of Felix Hoppe-Seyler calls to remembrance the *Zeitschrift für physiologische Chemie*, the first journal to be founded for the publication of papers of exclusive physiological chemical interest. In 1877 Hoppe-Seyler in collaboration with Baumann in Strassburg, Gähtgens in Rostock, Gorup-Besanez in Erlangen, Hüfner in Tübingen, Huppert in Prag, Maly in Graz, and Salkowski in Berlin issued the first number of the journal which has since become such a source of strength for the science it represents. In the introduction to the first number attention is called to the fact that the time has arrived for recognition of physiological chemistry as a distinct science, and the establishment of Hoppe-Seyler's *Zeitschrift* is in no small measure responsible for such recognition. At this time (1877) there existed no separate laboratories for physiological chemistry; one of the first was that of Hoppe-Seyler in Strassburg. Hoppe-Seyler's attention was early directed to the desirability of improvement in the chemical methods then in use and the possibility of making new ones. Methods for analysis of milk, bile, serous fluids, urine, blood, proteins, etc., are in many instances due to the work

of Hoppe-Seyler in large measure. He rendered particular service in the application to physiological chemistry of the physical methods employed in spectral analysis, polarization, methods of gas analysis as practised by Bunsen, and the colorimetric principles put forth by Vierordt and Hüfner. In 1858 appeared the first edition of his "Handbuch der physiologisch- und pathologisch-chemischen Analyse" which was translated into all the modern languages. Not less well received was the large work on "Physiologische Chemie" which appeared in 1877. His investigations upon blood and blood pigments were particularly important and began with the discovery of the absorption spectrum of blood. He was also greatly interested in the oxidative processes of the organism, and in the study of metabolic changes under pathological conditions. His attention was early attracted to the chemistry of the cell and under his direction was begun a series of investigations on cholesterol and lecithin as well as Miescher's work upon nuclein which later was so fruitful. Hoppe-Seyler also contributed largely to our knowledge of the chemistry of urine. Thus his work on indican, the aromatic acids, phenols, cresols, etc., from putrefactive processes in the intestine, the origin of hippuric acid, etc., attest to his activity in this direction.

The study of the chemistry of nervous tissue was begun in the latter half of the nineteenth century and the names of Liebreich, Diaconow, and Thudicum are especially associated with the early development of our knowledge concerning this type of tissue.

By a combination of the principles employed in chemistry, histology, and physiology Rudolph Heidenhain (1834–1897) in Breslau revolutionized the then prevalent ideas relative to the processes of secretion. His histological study of the structure of the pancreas wherein he showed the changes in the gland cells that accompany secretion, together with the work on the formation of pepsin in the pyloric glands and in those of the fundus, remain as standard examples of this type of investigation. Particularly significant were his experiments on lymph formation and urine secretion. His method of isolating the cardiac end of the stomach in order to collect its secretion was the beginning of the modern method of research in this direction. In 1883 appeared his classical essay "Physiologie der Absonderungsvorgänge" in Hermann's Handbuch der Physiologie. A defense of vivisection published in 1879 was reproduced in 1884 by direction of the Prussian Minister of Education.

The modern idea of the nature of protein digestion was conceived by a pupil of Claude Bernard, Willy Kühne (1837–1900), who first suggested that protein disintegration proceeds by a series of progressive hydrolytic cleavages. For our present nomenclature of the protein derivatives we are indebted to Kühne as well as for the term "enzyme" as a designation of digestive agents. Although the chief contributions to physiological chemistry from Kühne's laboratory at Heidelberg relate to the chemistry of digestion, his work on blood is equally well known, especially the fact that in 1865 he first isolated hemoglobin in a crystalline form. His text-book on physiological chemistry was at that time the standard work on the subject.

It was the researches of Edmund Drechsel (1843–1897), that initiated a new phase of protein chemistry. He first isolated lysin, the hexone base, from among the products of casein disintegration and thus opened up a field of new possibilities in various aspects of intermediary metabolism. His second base lysatinine, or lysatine, was of particular interest since it indicated the possibility of a direct formation of urea from protein. It had long been known that urea was the chief end-product of nitrogenous metabolism but the observation that urea was produced on decomposition of lysatinine pointed to this compound as one mother substance of urea. Later researches have demonstrated that lysatinine is identical with compound now known as arginine, which was studied by Kossel.

With the name of Marcelus Nencki (1847–1901) is associated a series of investigations on various phases of intermediary processes. From his laboratory at St. Petersburg were sent out many contributions to the knowledge of the behavior in the body of a varied list of organic compounds, especially those belonging to the aromatic series. Perhaps the best known and most significant piece of work completed by Nencki was his investigation on urea formation and the rôle of ammonium salts. The results of this research form the basis of our present conceptions concerning this type of intermediary metabolism.

At Berlin and Freiburg, Eugen Baumann (1846–1896), a pupil of Hoppe-Seyler, devoted himself to the task of elucidating the significance of sulphur compounds in the organism; the intermediary processes concerned with various aromatic compounds and their manner of elimination; the significance of the so-called conjugated sulphates; the chemistry of the diamines; various aspects of intestinal putrefaction, and the relation between the indole of the intestine and urinary indican was made plain. Furthermore, our knowledge of cystinuria we owe in large measure to Baumann. By his investigations he was led to the synthetic formation of various hypnotics now widely used in medicine, namely, sulphonal, trional, tetronal, etc. Iodothyrin the active principle of the thyroid glands was discovered and isolated by Baumann.

The influence of Ernst Salkowski (born 1844), a pupil of both Kühne and Hoppe-Seyler, upon the progress of physiological chemistry has been manifested in many directions, evidenced by a mere recital of the several lines of work in which his interest was exhibited. From his laboratory at Berlin have come a large number of acceptable methods for the analysis of urinary constituents and other fluids of the body, and his "Practicum der physiologischen und pathologischen Chemie" is widely employed. Among other types of investigation carried through by Salkowski may be mentioned studies on putrefaction, acid intoxication, urea formation, hippuric acid synthesis, problems in digestion, etc.

In the United States physiological chemistry was practically unknown until about 1880 when the first laboratory for the pursuit of this science was opened at the Sheffield Scientific School of Yale University. Russell H. Chittenden on his return from Germany, where he was a pupil of Kühne, offered courses in physiological chemistry which were modeled after those given in Europe. It is true that previous to this time courses in medical chemistry were given at various medical schools but these had little resemblance to the modern physiological chemistry. The establishment at New Haven of this course of study was unique, inasmuch as it was made a part of a preliminary training in biology preparatory to medical study and was not simply a course in the medical curriculum. Some of the best-known medical men and representative physiological chemists have received training in this laboratory. The research work for which the laboratory has been especially noted has been that relating particularly to the chemistry of digestion and other special phases of metabolism.

In the above brief sketch of the later development of physiological chemistry no attempt has been made to include the names of all the investigators whose work has been worthy of mention. Space forbids such a treatment and the names selected are those of men who have contributed to the science by both research accomplished and the influence still felt in the work of the large number of pupils who surrounded them.

In the last decade or so the science under discussion

has grown with great rapidity. With growth has come more or less specialization along various lines. The subject is now so broad that it is practically impossible for one individual to be a master of the entire field. Hence at present, so far as research is concerned various laboratories direct their energies into one or more highly specialized lines of work, as for example, problems relating to digestion or carbohydrate metabolism. This has continued to the point where to-day a given laboratory has come to be identified with a particular more or less limited field of investigation,

The multiplicity of discoveries and the mass of facts that have accumulated within the last twenty years relative to physiological chemical problems make it an impossible task to do justice to all lines of progressive investigation carried through. On the other hand a few types of work stand out so prominently and have been of so much significance in the very recent growth of the science that they must at least be mentioned. The investigations of Emil Fischer on the carbohydrates, the purines, and the proteins have caused an entire rearrangement of ideas with respect to varied phases of nutritional processes. The conception of a humoral path for the conveyance of chemical substances that exercise special regulation over physiological functions, as exemplified in the "hormone" or "chemical messenger," "secretin" by Bayliss and Starling; the work of Pawlow on digestion; the newer conceptions of cellular metabolism; of enzyme activity; the ideas of Loewi, Abderhalden, and others, concerning the synthetic powers of the animal organism; the changing views of the food values of various foodstuffs during growth and adult life; the methods for urinary analysis elaborated by Folin together with his theory of protein metabolism; Chittenden's investigations on the minimal quantity of protein compatible with health and vigor, the development of adequate ideas of the rôle of the purines, the interest in the interrelation of inorganic salts and biochemical processes, as exemplified by the work of Loeb and others, the inroad of physical chemistry, the great recent progress in the chemistry of fermentation initiated by the researches of Buchner, the more definite knowledge of the chemistry of the cell as developed by Kossel, the winner of the Nobel prize, all these are but indications of work accomplished in recent years.

The future development of physiological chemistry cannot be foretold, for as yet only a few of the fundamental principles have been touched upon and the field is immensurable. The progress of the exact sciences is constantly bringing new methods to the physiological chemist and their application is continually throwing more and more light upon the problems of nutrition. Until each detail of nutrition is known this science will not have completed its mission. However, in the progress of medical knowledge it will undoubtedly be found that physiological chemistry will occupy a more and more conspicuous position.

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Chemotaxis.—Microorganisms are attracted or repelled by certain chemicals. This phenomenon is known as chemotaxis, attraction being called positive, and repulsion, negative chemotaxis. All varieties of bacteria do not respond alike to this influence, for example, oxygen attracts aerobes but repels anaerobes. For the majority of organisms, however, peptone and urea exhibit positive chemotaxis, while alcohol and metallic salts repel them. Positive chemotaxis is not always a favorable influence for the bacteria, for many are attracted by a mixture of peptone and bichloride which is strongly poisonous to them. It has been thought that the leucocytosis resulting from an infection is due to the fact that the bacterial poisons possess some attractive force for the leucocytes and that the leucopenia, seen in some infectious diseases, is an example of negative chemotaxis. The chemotactic influence of any given chemical substance may be tested roughly by filling with it a fine capillary tube, placing the tube in a drop of the culture and examining it under the microscope in the form of a hanging drop. The accuracy of such an observation is of course impaired by the amount of diffusion which may take place.

Bacteria not free to move may respond to chemical influences by directing their growth toward or away from the active chemical. This is called chemotropism and is closely allied to chemotaxis. The form taken by a colony of mould or bacteria when grown on solid media is frequently determined by this influence, the active substance in this case being some body excreted by the organism.

RALPH G. STILLMAN.

Chemotherapy.—Under this term is understood the use of some chemical preparation for the destruction of pathogenic organisms infecting an animal body. It has of course been long known that microorganisms are very susceptible to the action of chemical poisons, so-called bactericides, and are easily destroyed when exposed to them in certain concentration in the test-tube. In fact, two substances have been discovered in an empirical fashion that have proved to be eminently chemotherapeutic agents in the new sense; they are quinine and mercury, the so-called specifics of the old pharmacopœia. Both these substances act directly upon the causative organisms of malaria and of syphilis and thus cure by freeing the body of these organisms. They were used for years before the infectious nature of the diseases in question was recognized and before their specific action could be demonstrated in any other but clinical fashion. It seemed as if bactericides should prove as useful in other infections as these two substances in malaria and syphilis. It was soon found, however, that the available preparations so far as tested had either no such specific effect upon the organisms or had just as destructive effect upon the body cells as upon the infecting bacteria. Surely mercury bichloride or solutions of formaldehyde in sufficient concentration can destroy all infecting organisms, but the amount necessary for such action would result in death of the animal by poisoning even before the death of the infecting bacteria.

ORGANOTROPISM AND PARASITOTROPISM.—The work of Ehrlich has been especially aimed at the overcoming of these difficulties and this at a time when serotherapy attracted almost the exclusive attention of the medical workers both in the laboratory and in the clinical fields, and the use of drugs, other than the old specifics, in the treatment of infectious diseases was scoffed at. Ehrlich saw early that therapeutic substances in order to destroy the organisms must go into chemical combination with them; they must have a certain affinity for the bodies of the organisms, must *anchor* them in other words. Such substances Ehrlich termed *parasitotropic*. But we have seen above that the known bactericides were poisons as well, that is they were *organotropic* as well as *parasitotropic*. The problem then was to find substances that should be preeminently parasitotropic and not at all or only very little organotropic when introduced into an infected animal body. The best objects for the experimental study of such substances proved to be trypanosomes: they could be plainly observed under the microscope, their death could be easily diagnosed by cessation of their movements, they were not apt to cause a high degree of immunity in the animals used for experiments, thus interfering with the study of the results of medication, and they were pathogenic for certain animals used in laboratory research.

NUTRIRECEPTORS AND CHEMORECEPTORS.—The hundreds of drugs that were used in combating infection with trypanosomes could be gathered into three distinct groups: (1) The group of arsenic compounds, arsenous acid, atoxyl, arsacetin, arsenophenylglycin, etc.; (2) certain azo dyes, trypan red, trypan blue, trypan violet; and finally (3) certain basic triphenylmethane dyes, parafuchsin, methyl violet, pyronin, etc. Ehrlich much earlier assumed that the molecules of living protoplasm are provided with various chemical combinations which are able to act fairly independently of the whole body of the parasite in relation to the substances found in the life medium of the parasite. He called these chemical entities "side chains" borrowing the name from the terminology of organic chemistry. Such chemical complexes were utilized by the parasite in grasping and assimilating the food particles found in the surrounding medium and hence acted as *nutrireceptors*. Later Ehrlich came to think that similar chemical substances were the acting elements in the reactions between drugs and the body of the parasite and therefore gave them the broader term *chemoreceptors*. When a drug was brought in contact with a given protozoon, whether in a test-tube or in the animal body, the following results were found to take place:

1. No reaction occurred between them; this of course meant than the protozoon possessed no suitable chemoreceptors and the drug was inert, was not a "poison."

2. Parasites combined with the drug, were either inhibited in their life processes or completely destroyed. This meant the existence of suitable receptors which were active both in the test-tube and within the animal body.

3. Parasites combined with the drug when *in vitro*, but not when free in the animal body. This striking result showed the great differences in the behavior of some drugs under different conditions. Thus Hata, a coworker of Ehrlich, found that methylene blue had almost unlimited power of inhibiting the life processes of the spirochetes of relapsing fever when brought in contact with them in a test-tube but proved to be completely inert in the animal body. The explanation was that the preparation in question and any similarly acting drug was more organotropic than parasitotropic and was prevented from acting upon the infecting organisms by being quickly bound to the cells of the animal.

4. No reaction occured *in vitro*, but binding of the drug by the parasites took place *in vivo*. Atoxyl is an example of a drug acting in this paradoxical manner and the explanation assumed by Ehrlich was that the drug in question underwent some chemical change in the animal body resulting in the appearance of a related substance for which specific chemoreceptors existed in the body of the protozoon. This assumption was later proved to be correct by the successful manufacture by chemical means of a substance derived from atoxyl which proved capable of destroying the parasites both in the test-tuble and in the body.

SERUM-FASTNESS AND DRUG-FASTNESS.—The study of the action of the drugs named above upon parasites led Ehrlich to the discovery of another phenomenon which has proved to be of the greatest significance in the therapeutic application of various remedies and even in the explanation of certain characteristic features of infectious diseases. He discovered that by treating parasites with any member of the drug groups mentioned above he could lead to the appearance of strains which were no longer susceptible to the inhibiting or destructive influence of the drug in question, though they remained quite susceptible to other members of the same group or to the influence of any members of the other drug groups. Such resistant strains of parasites became *chemofast*, to follow Ehrlich's phraseology, this property being analogous to the serum-fastness of parasites which were treated by the antibodies developed by the infected animal or by other animals. To produce serum-fast strains all that was necessary was to expose the parasites to the influence of sublethal doses of the specific antibodies, the result being a sudden appearance of a resistant strain, this appearance being

analogous to the well-known mutation in heredity. This new characteristic of the parasite was proved to be due to atrophy or disappearance of the specific receptors in the body of the parasite which made the antibody circulating in the blood a completely indifferent substance so far as the new strain of the parasite was concerned.

The explanation of *chemo fastness* seems to be quite different. Instead of disappearance or atrophy of certain receptors there takes place a change in certain chemical functions of the receptors which saves the parasite from forced combination with the drug or from *fixation*. The affinity of the parasite is so reduced, in other words, that the balance is again in favor of the body cells and the latter take up the drug before it reaches the parasite. Such accommodation of the parasite shows of course the wonderful economy of nature for it prevents the total loss of receptors which may exercise other functions while deprived of their capacity of combining with the special substance. The difference in the action of antibodies and of certain drugs in the rapidity with which resistant strains are developed and in the nature of such resistance is explained by Ehrlich by the assumption of "fleeting" and "sessile" combination between the parasite and the substance; antibodies apparently go into prolonged combination with the parasite, penetrate it in other words most effectively and lead to a complete loss of a receptor; certain drugs, on the other hand, simply damage or modify the nature of a receptor.

These considerations, all of which were experimentally proved by Ehrlich, throw a great light upon the nature of relapses. These are simply due to the development of strains resistant to the antibodies developed in the serum, and the number of relapses is simply the index of the number of such resistant forms that the parasite may be able to assume. Of great interest is the fact that this acquired characteristic of the parasite is transferred for many successive generations if reproduction takes place by simple division; it is immediately lost when sexual conjugation takes place. Serum-fast parasites lose this fastness when passed through a fresh animal; drug-fast organisms may lose it when a chance for sexual reproduction is given by the passage of the resistant strain through an intermediate host of the parasite. Thus a trypanosome—*Trypanosoma lewisii*—lost its acquired resistance to arsenical preparations after being passed through the body of a louse infesting certain species of rats.

The cure of any relapsing infection is possible, then, when the body develops a sufficient variety of antibodies to destroy the various resistant strains that the parasite in question is able to assume in its struggle for self-preservation; or when a sufficient variety of specific drugs is at hand to effect a similar purpose. Of course, the possibility exists that the body of the host may succumb in the interim because of the damage to its vital cells by the parasite, by the drugs used, or by the effects of the chemical combination between the parasite and the specific antibodies or drugs.

Therapia Sterilisans Magna.—In the search for more effective means than the above fractional method of destroying parasites, Ehrlich was led to formulate the effects aimed at in the following words: "My therapeutic program consisted in producing the homologue and derivative, in the most varied ways, of substances with a certain efficacy, testing the effect of each and then relying on the results obtained, to attempt to get better and better curative substances. This means, therefore, learning to shoot (to take aim), and to do so through chemical variations." The end of such endeavor is the complete sterilization of the infected animal body by the single introduction of a sufficient amount of a drug having special affinity for the parasite in question, in other words *the apt shot or magic*. That such therapy need not be an idle dream has been amply proved by Ehrlich in the case of numerous animals inoculated with various strains of trypanosomes or spirochetes. Well-authenticated results of similar nature have been reported in the case of man since the appearance of Ehrlich's salvarsan, though it must be granted that such results have been the exception rather than the rule in the use of this drug or its derivatives. On the other hand, the results obtained with fractional sterilizing therapy have fully justified combined medication in certain infections, as for instance the use of mercury and of salvarsan in syphilis, and have pointed the way to further successes in similar fields.

The reader is referred to articles on salvarsan and on the therapy of syphilis to learn of the practical application of the lore of chemotherapy developed by Ehrlich and his coworkers, the main tenets of which are sketched above. The great promise lies, however, not so much in the practical results already obtained, as in the fact that the production of a specific drug curative of an infectious disease has been due not to an accidental finding, but has come about as a logical outcome of theoretical considerations and of well-planned work founded upon such considerations. B. Michailovsky.

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Chenopodium.—*American Wormseed; Ansérine vermifuge* (Fr. Codex). The dried ripe fruit of *Chenopodium ambrosioides* L. or of *C. anthelminticum* L. (fam. *Chenopodiaceæ*).

The first-named species is the old-fashioned garden plant *Mexican tea* or *Ambrosia*, native of tropical America; the second appears to be of European nativity. Both are common weeds in the Eastern United States, growing along roadsides, about wharves, lumber yards, etc., and are of a sprawling and ascending habit, reaching a height of two or three feet. They have a strong, heavy odor, disagreeable to most people. The fruits, generally called "seeds," are utricles nearly one-twelfth of an inch (2 mm.) in diameter, depressed-globular, glandular, dull-greenish or brownish, the integuments friable, containing a lenticular, obtusely edged, glossy, black seed. This seed has a peculiar, somewhat terebinthinate odor, and a bitterish, pungent taste.

Chenopodium is now scarcely employed in medicine, except for the extraction of its one to two per cent. of volatile oil, which is its active constituent.

Oleum Chenopodii, *Oil of Chenopodium* or of *American wormseed*, is defined by the U. S. P. as a volatile oil distilled from *C. anthelminticum*. It should be distilled from the fruits but is usually taken from the entire plant.

Great care should be taken to distinguish between this and the oil of Levant wormseed (See *Santonica*), as well as between the two drugs. This is a thin, and, when fresh, colorless liquid of aromatic odor and bitterish taste; specific gravity, 0.965 to 0.985 at 25° C. (77° F.). It is slightly levogyrate, and should dissolve in five parts of seventy per cent. alcohol.

Like most aromatic herbs, chenopodium, in small doses, is a stomachic tonic; in large doses it is irritating and nauseating. The property for which it is mostly prized is, however, its poisonous action upon intesti-

nal worms, particularly upon the lumbrici. From five to fifteen drops of the oil in emulsion or on sugar is the usual range of doses.

Toxicology.—Oil of Chenopodium is a very powerful poison in overdoses. The symptoms are chiefly referable to intestinal irritation and cerebral congestion. There are drowsiness, great thirst, abdominal pain, perhaps with vomiting, intense sensitiveness to light and sound, but with indistinctness, aphasia of both kinds, stupor, coma, and death. The treatment is stomach evacuation, purging, with watery stools, free administration of water, enemata, brandy, and external heat. H. H. Rusby.

Chequen.—*Chekan.* The leaves of *Eugenia chequen* Molino (fam. *Myrtaceæ*). A large and beautiful white-flowered shrub of Chile and Bolivia, closely resembling the common European myrtle. The leafy twigs were originally used, but in this form by far the greater portion is inert woody fiber. The leaves average about half an inch or more in length, frequently with an obscure tooth on one side, thick, coriaceous, bright green, smooth, and punctate, and aromatic in taste and odor. They contain four or five per cent. of tannin and two or three of volatile oil, the latter consisting chiefly of pinene, with some cineol. Chequen belongs, therefore, to the Eucalyptus series of aromatic drugs, its action being specially upon the respiratory mucous membrane, through which the oil is largely excreted. Its use is as a tonic expectorant, particularly in catarrhal conditions. It is commonly given in the form of the fluid extract, in doses of fl. ʒ i.–ij. (4.0–8.0). H. H. Rusby.

Cherry, Wild.—See *Prunus Virginiana.*

Cheselden, William.—Born in Burrow-on-the-Hill, Leicester County, England, in 1688. He began the study of anatomy in 1703, under the celebrated anatomist Cowper, and at the same time he followed the surgical instruction given by Fern, the Surgeon-in-chief of St. Thomas' Hospital. He was only twenty-two years of age when he began giving public lectures on anatomy, and he continued this course of instruction for a period of twenty years. The great reputation which he secured by these lectures and the skill which he displayed in his surgical operations made it easy for him to obtain the place left vacant at St. Thomas' Hospital by Dr. Fern. At the same time he received the appointment of Consulting Surgeon to St. George's Hospital and that of First Surgeon to the Queen. He died on April 10, 1752, after a second attack of cerebral apoplexy, the first one having occurred three months previously.

Although Cheselden was a distinguished anatomist, posterity will remember him chiefly on account of what he accomplished as a surgeon. The titles of his principal publications are the following: "Anatomy of the Human Body," London, 1713; "Treatise on the High Operation of the Stone," London, 1723. A. H. B.

Chest.—See *Thorax.*

Chest, Deformities of the.—The chest is a box or cage enclosing and protecting the heart, lungs, and great vessels; but it is also an organ, which by its rhythmical expansion and contraction plays an important part in the respiratory act. It consists of the thoracic skeleton and of the soft parts covering it; but the position of the clavicles, scapulæ, and shoulders is so closely related to the shape and development of the chest as to require some discussion in this article.

The size, shape, and mobility of the chest vary with the race, age, sex, development, occupation, activities, habitual postures, clothing, and idiosyncrasies of the individual, and it is as difficult critically to define its normal limits as it is those of the nose, ear, or any other organ or part. It is often impossible to say when normality becomes peculiarity, or peculiarity deformity.

According to Vierordt,[1] one expects to find in a well-constructed thorax, bilateral symmetry, slightly marked supraclavicular depressions, and a barely recognizable prominence at the junction of the manubrium and corpus sterni. The true ribs should so leave the sternum that there is increasing obliquity from above downward, making the angle between their free borders almost a right angle. The thorax should be well developed, and the scapulæ should lie flat upon the back; only the lower intercostal spaces should be visible. The dimensions of the chest should be proportionate to the size and development of the body, and in adult life its transverse diameter should exceed its antero-posterior in the ratio of three to two or less. Vierordt's Tabellen[2] give various chest measurements according to the most reliable observations. The mean value of chest play, or the difference in chest circumference between inspiration and expiration, is thus given as three or four inches. According to Lee,[3] the average expansion of the chest in eight hundred United States recruits was three and four-fifths inches.

Departures from the typical standard are very frequent, and may be quite marked in perfectly healthy persons. The two sides are rarely perfectly symmetrical; indeed, Vierordt himself says in another place that in right-handed people the right semicircumference of the chest is the larger by 0.5 to 2 cm.; in the left-handed, on the contrary, the left semicircumference of the chest is equal to or but slightly greater than the right. The chest may be small above and wide below; the angle of Louis may be more than usually prominent, and the epigastric angle exceptionally acute. The supraclavicular fossæ may be marked, without disease; but if they are unequal, apical tuberculosis may be suspected. Certain ribs, as the second, third, and fourth, may project in front, or the lower ribs may be depressed. All these peculiarities are more or less atypical without being exactly abnormal.

The broad chest of man with the square shoulders, and scapulæ placed posteriorly, correlated with the upright posture and pendant, but freely mobile and active arms, is one of the most characteristic and striking peculiarites of the human skeleton. According to Hutchinson,[4] this position of the scapulæ is a very important factor in the development of respiratory power. Human respiration is, or should be, bellows-like, the fixed flap being the spine and posterior chest wall, rather than piston-like, as it often is in cramped or rigid chests.

In the human embryo at the fourth month the quadrupedal or deep chest, with the anteroposterior diameter exceeding the transverse, still persists; at birth these diameters are nearly equal. The infant is round-chested and round-bellied, and only after three or four years of age do the chest and abdomen begin to assume the more flattened shape characteristic of adult life. In adult man the proportions of the chest are the reverse of those in the quadruped, the transverse exceeding the anteroposterior diameter in the ratio of three to two or less. Of the quadrupeds only certain monkeys, moles, and bats, all animals possessing great power and freedom of motion in the anterior extremities, have broad chests. The evolution of the human chest may be arrested before it is complete, either from congenital defect in growth or vigor or from faulty habits in childhood; we then get a long, rounded chest, a degenerate or rudimentary type, and one often associated with other defects, as will be pointed out in the sections on the phthisical chest and on round back.

Chest deformities may be divided for convenience of discussion into four groups: the congenital; those due

to static conditions, whether pathological or not; those due to external constriction or pressure; and those due to conditions of the internal organs. Deformities of the chest due to violence, to new growths, to local disease, or to double or non-viable monstrosities, are beyond the scope of this article.

I. Congenital Deformities.—The individual bones of the chest may be imperfect or wanting, fissured, misshapen, or augmented, and the thoracic skeleton may be deformed as a whole.

Spine.—The thoracic spine, like the cervical and lumbar, may contain too many or too few vertebræ. Dwight[6] states that since he has been looking for such anomalies, he has found them with surprising frequency. The commonest anomaly of number in the dorsal region is to have eleven or thirteen vertebræ present. Noble Smith[7] quotes a case in which four and one-half thoracic vertebræ were absent, namely, the right half of the third, and the fifth, sixth, eighth, and ninth. There were only two cervical vertebræ present in this case. Wedge-shaped half vertebræ on one side or the other, as in the above case, are not extremely rare; or a vertebral body may be made up of two unfused halves. The arches may be incomplete—spina bifida—a condition which may extend to a great part or the whole of the spine, and is then called rhachischisis, with which, as with ordinary spina bifida, protrusion of a sac and various anomalies of the soft parts frequently occur. In these cases various abnormal and often extreme bendings and curves of the spine and accompanying chest deformities are often seen. A good paper on rhachischisis is that by Thorndike.[8]

Putti[47] has an exhaustive paper on vertebral anomalies with literature up to 1910.

It is well for bone specialists to remember, and probably for others to forget, the possibility of anomalies in number when counting vertebræ in the living subject; also that one or more spinous processes may be bifid, or project to one side or posteriorly without pathological significance.

Sternum.—According to Dwight,[6] the sternum is about 9.5 per cent. of the total height for men and about nine per cent. for women. It may be entirely or partially absent, or more or less fissured longitudinally or perforated. These defects, like the unclosed arches of a spina bifida, are due to the failure of the primitive layers to unite in the median line. When large the gap is covered by a membrane; when small it may be entirely unnoticed during life. Holes, fissures, and defects are more common and of greater extent toward the upper part of the sternum. The xiphoid is often deflected, split, or perforated.

Ribs.—Supernumerary ribs may occur, especially in the lower cervical and upper lumbar regions. Cervical ribs on one or both sides may sometimes be palpated at the root of the neck during life, and may cause trouble by pressure on the brachial plexus and require removal. In these cases the pleural sac may rise abnormally high, and has been opened (Planet[9]). Ribs may also be absent or rudimentary. Cases of complete absence are rare; a case has recently been reported by Carroll Smith[48] of complete absence of the left seventh and eighth ribs in a syphilic infant. The left arm fitted accurately into the depression at the side of the chest. Hurtlet[10] reports five cases of rudimentary first ribs in English, and Helm[11] sixteen cases in general surgical literature. Cases occasionally occur in which several ribs on one side with their costal cartilages are imperfectly developed and fail to meet and unite with the sternum, or in the case of the lower ribs with the cartilage above, by varying intervals. They may end near the sternum or free border, below the axilla, or farther back, leaving a depression or furrow of greater or lesser extent at one side of the sternum, or in the lateral chest wall, covered only with skin and membrane; this may rise and fall with respiration, pulsate with the heart beats, and through it the underlying organs may be palpated. Through this unprotected area the lung may protrude, or if in the precordial region an ectopia cordis may take place. When such a tendency exists the gap should be protected by a celluloid, hard-rubber, or metal plate, and pulmonary hernias have been known to recede under such treatment, or to disappear spontaneously. These defects of the skeleton of the chest wall are due to an arrest of growth of fetal structures, which fail to join by a larger or smaller interval.

The following cases are cited as examples of this deformity:

Abercrombie's[12] case was in a boy of two months, with absence of the second and third costal cartilages, left side; the corresponding ribs ended free, leaving a small unprotected space. The fourth rib lay near its cartilage, but was not joined to it. There was a notch on the left side of the sternum near the third interspace.

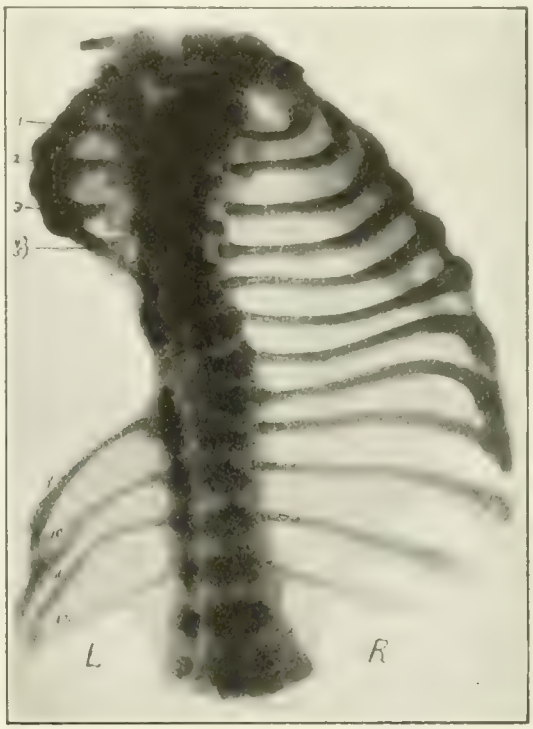

Fig. 1353.—Dr. Carroll Smith's Case of Total Absence of the Seventh and Eighth Ribs on the Left Side. (*Journal of the American Medical Association*, March 22, 1913).

Bennett's[13] case was that of a man who died suddenly after an injury. The autopsy disclosed a defective third rib, right side, which failed to reach its cartilage by a considerable interval. This case and another reported by Bennett emphasize the danger of mistaking certain congenital chest deformities for the effect of injury, recent or remote.

Osborne's[14] case was in a boy with a triangular depression on the left side of the chest due to defective development of the second, third, and fourth ribs, which were separated from their cartilages by a considerable interval. The extremity of the fourth rib was joined to the fifth costo-cartilaginous articulation.

In Townsend's[15] case the ribs of the left side, except the first two, were represented by short rudimentary processes.

Lallemand's[16] case was in a man who had a depression as big as a fist on the left side of the chest, due to a deficiency of the third, fourth, and fifth ribs.

Harold's[17] case was that of a backward boy of seventeen years, whose costal cartilages in the left side below the fifth rib were missing; at this level the left half of the sternum and xiphoid were deficient, and the pericardium was protected only by soft parts.

Homer Gage[18] reported a case of congenital absence of the sixth, seventh, eighth, ninth, and tenth ribs, left side, in a girl of seventeen years. There was severe lateral curvature, convexity to the right, with marked deformity of the chest, and a protrusion in the

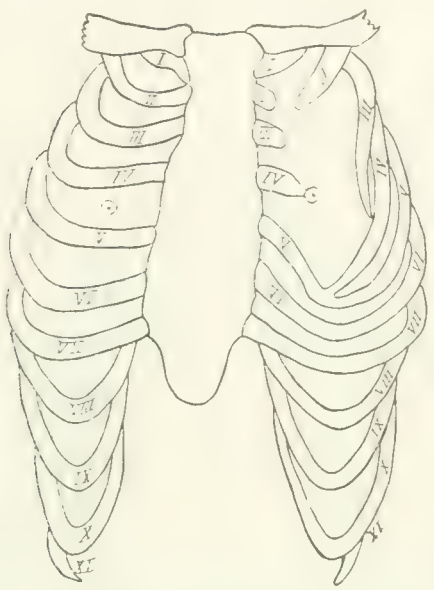

Fig. 1354.—Osborn's Case of Defect of Ribs. (From Haynes).

unprotected area, supposed to be due to a hernia of the stomach. The heart was displaced to the right, though the viscera were not transposed.

In Hayne's[19] case the cartilage of the seventh rib, left side, ended three-fourths of an inch from the sternum, and the seventh, eighth, and ninth cartilages were not joined, but ended free.

Sometimes the costal defect is accompanied by total or partial absence of the greater and smaller pectoral muscles of the same side, as in the case reported by Levy,[20] in which the third and fourth ribs of the right side ended below the axilla, leaving a marked depression. There was a well-marked lateral curvature with convexity toward the right.

Schlesinger[21] has shown that congenital absence of the pectoral muscles is frequently associated with defects of ribs or other thoracic anomalies, and cites the case of a man of twenty-two years who had in addition to a defect of the third, fourth, and fifth ribs, and of the costal portion of the pectoral, a congenital elevation of the shoulder—Sprengel's disease—all on the left side. It would seem that defects in the costal apparatus are more common in males and on the left side, that they are frequently associated with other thoracic anomalies, and that they sometimes occur in individuals otherwise or generally defective.

Other thoracic deformities sometimes accompany congenital malformations of the heart; there may be in such cases a projection or gibbosity of the front of the thorax above the xiphoid, "thorax en proue," or "thorax en carène," or the thorax may be prominent in front with flattened sides (see Charrin and Le Noir[22]).

Occasionally there is a fusion of ribs, usually the first two, which are then sometimes called a bicipital rib. Other ribs may be fused at one or more points (*Deutsche Chirurgie*[23]).

The subject of rib anomalies is very thoroughly discussed by Kienböck[49] who divides them into the following groups:

I. Those associated with congenital elevation of the scapula.

II. Congenital costal deficiencies.

III. Cruveilhier's rib anomaly, where adjoining ribs are united by a long bony process.

IV. Luschka's forked rib, in which the anterior end of a rib usually the fourth or fifth, is forked.

V. Serb's sternum rib anomaly, where the anterior ends of the first and second ribs fuse and articulate with a bony process from the manubrium of the sternum.

Rib anomalies are frequently associated with congenital anomalies of the vertebræ and scoliosis.

Stiller's Costal Stigma, Costa Fluctuans.—Stiller maintains that the majority of cases of enteroptosis begin in youth and are associated with abnormally movable tenth ribs. This mobility may approximate that of the two lowest pairs of ribs, and is due to a congenital and possibly inherited defect in the cartilage which joins the tenth rib with the cartilage above. He claims that enteroptosis and nervous dyspepsia are identical, and that children exhibiting the costal sign will always go on to have enteroptosis, atony of the stomach, constipation, and nervous dyspepsia or dyspeptic neurasthenia. He finds these conditions nearly as common in men as in women, and concludes that tight lacing and pregnancy have but little to do with enteroptosis.

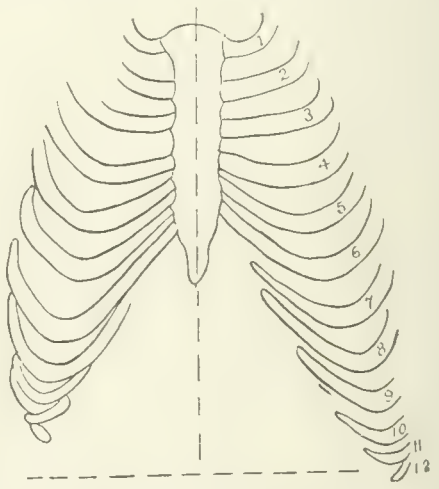

Fig. 1355.—Haynes' Case of Defect of Lower Ribs on the Left Side. (From Haynes.)

Absence of the Pectoral Muscles.—This deformity occurs more frequently on the right side, and may involve both the large and small pectorals, but the pectoralis minor and the clavicular portion of the former often escape. The affected side of the chest has a flattened or excavated appearance, but the patient has full use of the arm and suffers no inconvenience, and may even be a good soldier or gymnast. An infant six weeks old with absence of the costal portion of the left pectoral was exhibited by the writer to the Orthopedic Section of the New York Academy of Medicine in January, 1898, and by a singular coincidence a boy of sixteen years with the same deformity on the right side was shown at the same meeting by Dr. Royal Whitman. In these cases there are usually certain anomalies of the neighboring soft parts such as deficient subcutaneous tissue, scanty hair over the af-

fected area and in the axilla, imperfectly developed mammilla, breast, and anterior axillary border of the affected side. In certain cases defects of the ribs and anomalies of the scapula may exist, as in a case reported by the writer,[25] and in one described by Schlesinger,[21] who has collected one hundred cases of pectoral defect from medical literature, and who states that in about one-quarter of the cases the pectoralis minor is also absent; in one-tenth of the cases there is considerable anomaly of the thoracic skeleton, and in one case in twenty or twenty-five there is pulmonary hernia or displacement of the heart.

Funnel Chest, Funnel Breast, Trichterbrust, Thorax en Entonnoir.—This deformity is one of the most interesting of the congenital chest deformities, and has attracted considerable attention since Ebstein's[26] paper appeared in 1882, though the condition had been previously described. Stedman[27] gives the earlier references.

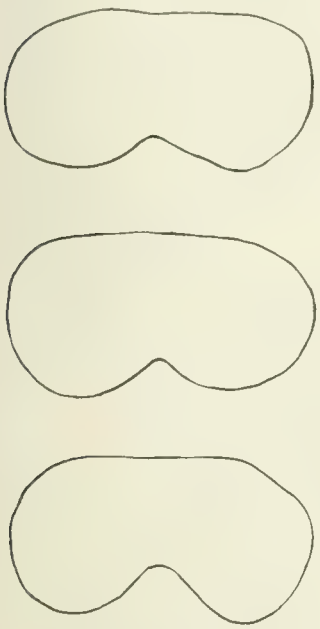

Fig. 1356.—Funnel Chest. (Arneill's case.)

In these cases there is a considerable depression involving the lower portion of the sternum, and the adjacent cartilages and ribs. This depression may be large enough to contain a man's fist, and is usually congenital, but its etiology is obscure. Some authors suppose it to be due to a defect in development, others to the pressure of the fetal chin or heels. Certain authors regard it as a stigma of degeneration, as it has been found in the insane, epileptic, and neuropathic; others have observed it in robust and well-developed individuals. It occurs more frequently in men; out of thirty cases twenty-three were male.

Arneill[28] reports six cases, of which five occurred in one family. These were a student, his brother, father, and two paternal uncles. This patient was twenty-five years old, six feet tall, and weighed one hundred and seventy-four pounds; he was well developed and in excellent health. In his case the antero-posterior diameter of the thorax was, at the right nipple 17.5 centimeters, at the left 16.8, and at the depression in the median line 11.4. The greatest depth of the depression was 6.5 centimeters. In the brother the depth was 4.7, and in the father 3.75. There was one sister who was free from defect. Of Klemperer's[29] three cases two were brothers. The writer has recently reported the cases of a mother and daughter.

Teterianz[50] reports a case of funnel chest with congenital metatarsus varus in a five-year-old boy. This rather strengthens the intrauterine pressure theory of causation.

A number of cases of acquired funnel chest have been reported. The deformity may be acquired by traction from within, from adhesions or bronchiectasis, or by pressure from without, as in certain occupations. An excellent account of this and other chest deformities may be found in an article by Marie.[30] As already noted, there is little or no interference with function, and some individuals are able to take violent exercise, as respiratory capacity does not seem to be diminished. Ebstein[26] has described some cardiac displacement upward and to the left.

Thorax en Gouttière.—Somewhat similar to funnel chest is the "thorax en gouttière" of Féré and Schmidt,[31] where the sternum forms the bottom of a longitudinal trough or gutter whose sides are the incurved costal cartilages. These authors claim that ten per cent. of epileptics show this deformity.

Clavicles.—The clavicles may be wholly or partly absent on one or both sides. In partial absence it is usually the outer extremity which is wanting. The shoulders drop forward and inward, and may even be made to meet in front, but there is surprisingly little interference with function. The writer's clavicle splint[32] may be used to keep the shoulders in position, acting on the principle of artificial clavicles.

Congenital Elevation of the Scapula, Sprengel's Disease.—This condition was first described by Sprengel in 1891, and is not yet thoroughly understood. An excellent discussion of the subject may be found in the paper by Nové-Josserand and Brisson,[34] who report twenty cases in literature and their own observation of a girl of nine years with the right scapula three centimeters higher than the left.

Fig. 1357.—Congenital Elevation of the Right Scapula. (Original.)

Besides being elevated the scapula was rotated so that the inferior angle was nearer the spine, and the spine of the scapula pointed downward and outward. The upper border of the scapula pointed upward into the neck, producing a noticeable deformity. The right scapula was somewhat smaller than the left, but the clavicles were equal. The movements of the shoulder-joint were free, but the arm could not be raised as high as on the opposite side. The muscles responded normally to electric stimulation. The above description is typical, and applies to most cases. In about

half the cases there is a slight scoliosis, of which the convexity may be from or toward the affected side.

In some cases there is facial and cranial asymmetry, the side of the elevated scapula being the less developed. The scapula itself may be short, wide, or small, and the arm of the affected side may be shorter and thinner. Defective and anomalous ribs and vertebræ and muscle defects are not very rare; the remainder of the opposite side may be small. There is little disability, sometimes none, and when treatment is required remedial gymnastics are sufficient. The writer[25] has reported a case of small scapula with absent pectoral muscle on the right side. This case seems to belong in this group, though the elevation of the shoulder was slight.

A peculiar form of congenital high shoulder, in which the scapula was joined to the spine of the seventh cervical vertebra by a bony process, has been described by Wilson and Hugh.[35] A number of cases of costiform bone connecting the superior angle with the spinous process of one of the lower cervical vertebræ have been reported since.

Congenital Scoliosis.—This deformity involves more or less all the bones of the thorax. The cases in which lateral curvature is congenital are rather rare, though Marie[30] thinks that many cases of lateral curvature which develop in childhood may be due to congenital defects of the thorax or spine, which remain latent or without visible effect for years, but finally produce a visible curvature. He includes such cases under the term "déformations thoraciques congénitales tardives." In a recent study Hirschberger[36] attributes a certain number of cases of congenital lateral curvature with defects of the spinal column to intrauterine pressure, with scanty amniotic fluid. Another group is associated with other anomalies, showing a widespread developmental fault. A few cases only are due to paralysis. The attention of the profession has lately been increasingly drawn by Böhm[51] and others to the considerable number of congenital lateral curvatures with rib and vertebral anomalies, and to the still larger number where a curvature, unnoticed until the first or second septennium, has its basis in a definite vertebral anomaly.

The chest deformities associated with lateral curvature will be more fully described in the following section.

II. Acquired Deformities.—(*a*) *Chest Deformities Due to Static Conditions.*—This group comprises the chest deformities due to the various forms of lateral curvature of the spine, weak and round back, to spondylitis, and in part to certain constitutional diseases affecting the bones, such as acromegaly, osteitis deformans, and spondylitis deformans. It should not be forgotten that the shape of the thorax is very intimately correlated with the activities and habitual or typal postures of the individual.

Lateral curvature of the spine, or scoliosis, is the name of a striking symptom, whose causation varies widely in different cases, and in many is exceedingly obscure. The list of diseases and conditions with which lateral curvature is more or less frequently associated is a long one, but in all the efficient cause is an asymmetrical or unilateral weakening of the skeleton or muscles, often due to a one-sided incidence of stress, as an habitual faulty or one-sided posture, loss of an arm, short leg, congenital defects of spine or chest, torticollis, Sprengel's disease, sacroiliac disease; in other cases to asymmetrical softening, hardening, or distortion of certain parts of the skeleton as in rickets, cretinism, achondroplasia, acromegaly, diffuse hyperostosis (leontiasis), osteomalacia, rheumatism, spinal osteoarthritis, osteitis deformans (Paget's disease), pulmonary osteoarthropathy, and often tuberculous spondylitis; also in certain nervous and paralytic disorders which affect the spinal and trunk muscles in an asymmetrical manner, such as poliomyelitis, sciatica, Friedreich's ataxia, syringomyelia, hysteria, athetosis, paralysis of certain spinal muscles, and some of the chronic muscular atrophies and dystrophies. The commonest and most important class, however, is that in which the lateral curvature is attributed to muscular weakness and habitual faulty postures, but in which no very obvious predisposing cause is evident and about the causation of which very little is really known.

The distortion of the spinal column is probably the most important but by no means the only element in the deformity. The entire thorax becomes by degrees warped and twisted, and while the different varieties of lateral curvature vary in their characteristics, and the ordinary or postural deformity in the degree of distortion finally reached, it is not too much to say that the severer grades are among the most distressing, and, unfortunately, the most common of severe chest deformities. In many cases the distortion or debility affects not only the trunk, but the pelvis, head, and extremities.

The spine usually has a dorsal and a lumbar curve in opposite directions. The convexity of the dorsal curve is to the right in a large majority of cases. The spine is also twisted on or near its axis in the same direction in which it curves, owing to its lying free from support in the thoracic and abdominal cavities:

Fig. 1358.—Chest Deformity in Severe Scoliosis.

the line of the vertebral bodies thus comes to be much more curved than the line of the spinous processes—in other words, the deformity is much severer and more complicated than it appears to be from external inspection. After the deformity has lasted some years, the bodies of the vertebræ become wedge-shaped and twisted, the intervertebral discs compressed, and the deformity becomes fixed. The development of this spinal distortion has a profound effect upon the shape of the chest, which becomes shortened in height, reduced in most of its measurements, and is rendered stiffer and less flexible. The ribs on the side of the dorsal convexity become more bent at their angles, making a projection under the corresponding scapula; this projection is sometimes

very prominent, producing a large posterior boss. The ribs on this side are more separated at the sides and in front and become broader, but are crowded together behind, where they may form false articulations with the spine and with each other. On the concave side the ribs become straighter and narrower, and there is a flattening or depression in and below the scapular region. The scapula is usually lower and less prominent on the side of the dorsal concavity, higher and more prominent with projecting inferior angle on the convex side. With a right dorsal convex curve, the left side of the thorax is prominent in front, and the left breast and left free margin of the ribs protrude; the diagonal from right back to left front

Fig. 1359.—Anteroposterior Chest Deformity in Severe Scoliosis. The posterior boss is on the right side only.

is much longer than normal, and exceeds all other horizontal measurements; the opposite diagonal is much shortened, and a horizontal transverse section of the chest shows an irregular ellipsoid, lying in the direction of the long diagonal. Both lungs are cramped, the right the most, breathing capacity is much diminished, the heart is displaced to the left, and the abdominal and pelvic organs are crowded. The direction of the sternum is changed, and the whole thorax and trunk are strangely shortened and twisted. It is strange that chronic pulmonary disease is so seldom met with in these severe cases of lateral curvature. They are, however, not strong, and do suffer from their deficient respiration and imperfect circulation in a delicate organization, poor blood, and defective nutrition. Satterthwaite[37] has specially studied the displacements of the heart due to lateral curvature, and Faber[38] the respiratory difficulties.

The foregoing description may serve to indicate the principal characteristics of the chest deformities accompanying the commonest form of lateral curvature. In the lateral curvature due to morbid processes affecting the osseous system, the bones of the chest will present, besides the deformities of lateral curvature, those due to the special morbid process, such as softening, hypertrophy, or local distortion. In paralytic lateral curvature there is less rigidity, and there may even be increased flexibility, and paralysis of certain muscle groups will be found.

For the symptomatology and treatment of lateral curvature, and for its effects on other parts of the body, the reader is referred to the article on that subject.

Chest Deformities Associated with Paralytic Affections.—The commonest is lateral curvature and its accompanying thoracic distortions, as mentioned in the preceding paragraph, and the commonest variety of paralytic lateral curvature is that associated with a certain number of the severe cases of acute poliomyelitis, in which the trunk or spinal muscles are asymmetrically involved.

In the progressive myopathies of the scapulo-humeral type, and of the facio-scapulo-humeral type, and in pseudohypertrophic paralysis, there often occurs, according to Marie,[30] a flattening of the upper part of the thorax. Atrophy of the pectorals in connection with this deformity causes the upper part of the chest in front to have an excavated aspect. In some cases this depression is found in the lower part of the chest giving an appearance similar to funnel chest, and these deformities may be combined with scoliosis. Certain of these atrophic affections produce a wasp figure, the obliquity of the ribs being increased, and the chest being straight at the sides and cylindrical, with a marked depression or constriction between the lower ribs and the thoracic crests, owing to atrophy of the waist muscles.

Round back, kyphosis, round shoulders, stoop shoulders, are faulty postures or deformities, in which the head, shoulders, and upper chest fall or sag forward, from improper poise and muscular weakness. The result is a rounded back, and consequent changes in the shape of the chest, position of the head and shoulders, and, indeed, a general fault of attitude, a de-energized position in which the principal stress is shifted from the muscles to the ligaments. There has been considerable confusion in the nomenclature and in the description of this affection, or rather symptom. Round shoulders is a term in common use, but is unsatisfactory since the faulty position of the shoulders is a secondary symptom, largely due to the shape of the back and chest, for which reason the term round back is preferred by the writer, though this term also fails to indicate the general disturbance of poise which is usually present. The term kyphosis is unfortunate, since it is also used to designate the deformity due to Pott's disease of the spine, from which it is exceedingly important to distinguish it.

Round back or weak back, then, is that position of relaxation into which the body falls when the upper trunk is no longer held up by the weakened spinal muscles. Excluding the angular projection of Pott's disease, which becomes rounded only in the latest stages, the affection may be divided into several varieties, namely, those due to: (1) Imperfect development of the chest: (2) congenital or acquired weakness—convalescence; (3) old age; (4) paralytic affections; (5) certain diseases which affect bone and general nutrition, such as rickets, scurvy, cretinism, osteoarthritis, or spondylitis deformans, osteitis deformans (Paget's disease), acromegaly, pulmonary osteoarthropathy. The list is very similar to that given for scoliosis, but whereas in that case the bony or muscular support was weakened on one side, in this the weakening is approximately symmetrical.

Most of these kyphotic conditions have in common the forward sagging of the spine for lack of bony or muscular support or both. The head and upper chest fall forward, the spine becomes more or less rounded, the chest becomes compressed at its upper part, but may become narrower rather than flatter as a whole; the ribs drop downward, the shoulders

and scapulæ downward and forward, their inner borders receding from the spine and their inferior angles becoming more prominent. The position of the pelvis is changed, the feet are weak or flat and everted, and there is a tendency to knock-knee. The chest is usually less flexible than normal, respiratory capacity and power are diminished; there is often a transverse furrow at the upper border of the abdomen. The attitude is that of fatigue, weakness, debility, relaxation. It is doubtless an attitude which may be produced or intensified by habitual faulty positions, such as those assumed for many hours daily by school-children or clerks at their desks. This factor, however, must usually be associated with fault of structure or inherited or acquired

Fig. 1360.—Severe Round Back. (Original.)

vice of nutrition, muscle tone, or skeletal resistance, in order to be effective. It is to be noted that the non-pathological form of round back often affects children as early as the fourth or fifth year, and that, as already remarked, it is rather a general than a local affection. Weak and pronated feet, weak eyes, and slight degrees of lateral curvature often accompany it. These children are often physically delicate and mentally unstable. They may inherit an imperfect physique, or their life is so precocious or intense as to interfere with ample and symmetrical development. In other words, a good many of these children are degenerates or bordering on degeneracy, and present the rounded back and drooping shoulders as striking symptoms, but usually show other unmistakable signs of imperfect development. The writer believes that in a certain proportion of these round-backed children, the evolution of the chest has been retarded or arrested at a certain stage either from inherited tendency or from causes acting in early childhood, irrespective of faulty attitudes, and that this rudimentary chest stands in close relation with the pretuberculous type of chest described by Hutchinson. It is probable that in a certain class of cases the faulty attitude is in large measure dependent on the long, narrow, and deep chest, which favors drooping shoulders and abducted scapulæ, and to the instinctive desire of the delicate, under-nourished, and over-stimulated child to shift the strain of bodily weight from the tired muscles to the insensitive ligaments.

It follows that purely local treatment rarely fulfils the indications, and that management with a view to general development and a proper regulation of the life is of primary importance. The chest should be amply developed in early years by a free, open-air life, with plenty of tree and hill climbing, romping, rambling, swimming, running, and ball-throwing, sports that involve well-distributed and vigorous exercise, and expecially develop arm action and respiratory power.

Fig. 1361.—Upper Dorsal Pott's Disease; Exaggeration of Chest Deformity From Wearing a Cabot Jacket. (Original.)

The habits should be regulated and overstimulation, avoided. When the chest deformity is pronounced, special corrective and gymnastic exercises are of great benefit. Remembering that the faulty attitude is general, it is often necessary to begin by strengthening, placing, and shoeing the feet, in order to secure a correct pose. Thus the pupil should be drilled in the proper poise of the body, chest forward and up, abdomen and hips back, weight on balls of feet.

After these matters have been attended to, breathing and corrective exercises may be successfully applied to the chest. Supporting apparatus is seldom, and shoulder straps are never, required. The senseless admonition to throw the shoulders back without attention to these preliminaries would be productive of much harm if it were not almost invariably disregarded.

The round back of certain occupations and that of convalescence are varieties of the round back of weakness. The round back of old age is accompanied by changes of form in the chest similar to those described. It is due to the gradually increasing muscular weakness and ligamentous rigidity due to advancing age. The spinal muscles, whose tonus is diminished, no longer suffice to hold the spine erect and the chest free. The drooping spine compresses the intervertebral discs anteriorly; their elasticity is impaired, and the false attitude finally becomes fixed. The only efficient prophylactic is an active and well-distributed muscular life in youth and manhood with the avoidance of debilitating influences.

In round back due to paralytic disorders the spine is often extremely flexible, though respiratory power is diminished from muscular weakness. The chest often remains collapsed, and the breathing may be abdominal. The management is usually that of the disorder upon which the round back depends. Special exercises and supports are sometimes of service, and the writer has found the prone position on an inclined padded board or mattress to have an excellent influence in stimulating the spinal erector muscles to action, and in correcting the deformity.

Fig. 1362.—Rounded Kyphos of Cured Pott's Disease. (Original.)

The round back of paralysis agitans is similar to that of old age.

The round back or so-called kyphosis of rickets, infantile scurvy, cretinism, and marasmus usually comes on in infancy before the child is able to walk, and consequently before the evolution of the normal anteroposterior curves of the spine. The sitting posture probably has much to do with its production, and the projection is of a different character from that described in the first part of this section. It is rounded and situated in the middle or lower part of the back, though it may involve nearly the whole spine, which is more or less flexible and free from muscular spasm; there is no characteristic pain. It differs in all these respects from the kyphosis of spondylitis, with which it is sometimes confounded, and which it is exceedingly important to differentiate. Mechanical support is rarely required, as the deformity usually recedes under recumbency for longer or shorter periods, together with the treatment appropriate for the dyscrasia. In the rare cases in which the deformity persists and becomes rigid after the cure of the disease, the treatment is difficult, and mechanical support may be required.

Fig. 1363.—Kyphos and Chest Deformity of Cured Pott's Disease. (Original.)

In acromegaly the dorsal spine may become rounded, and the ribs, sternum, and clavicles hypertrophied, giving a massive, deep chest. The bent back and exaggerated senile attitude may occur in osteitis deformans (Paget's disease) and in osteoarthritis of the spine.

Angular Kyphosis.—In Pott's disease the integrity of the spinal column is destroyed by local tuberculous ulceration, and the upper section of the trunk falls forward until it finds support, giving rise to a kyphos, or hump of the back, which is at first always angular, and to various changes in the shape of the chest, especially if the disease affects the thoracic vertebræ. In disease of the upper dorsal region the upper part of the chest is flattened in front. In disease of the mid-dorsal region the ribs become more sloping, in severe cases resting on the ilium or within the pelvis; the chest becomes shortened and laterally compressed; the sternum and lower ribs become prominent, and the anteroposterior diameter of the chest is increased. The chest also becomes very rigid, and the breathing abdominal and accelerated.

The changes in the shape of the chest take place very slowly, and are only fully developed after several years. There are always rigidity and spasm of the

spinal muscles during the active stage, and often restlessness or crying at night, abdominal pain, and a characteristic attitude. These points and others differentiate it from the rachitic spine already described. The treatment is that of Pott's disease, which includes attention to hygiene and nutrition, long-continued spinal support by special appliances, the avoidance of exercise, and more or less recumbency.

The Rachitic Chest.—Besides lateral curvature and kyphosis there are other deformities of the chest so frequently found in rickety children as to merit separate mention.

Harrison's Groove.—The greatest softening in the rachitic chest takes place in the cartilages of the lower ribs, where the chest is unprotected by the lifting action of the upper and lateral chest muscles. Just below the nipples there is nearly always a depression, which in severe cases extends upward near the costosternal junction or outward toward the axillary line. It has often been thought that this depression was due to the traction of the diaphragm, but it lies above

Fig. 1364.—Rachitic Chest, Showing Pigeon Breast and Harrison's Grove. (Original.)

the diaphragmatic attachment. The free border of the ribs is usually prominent, owing to enlarged liver and spleen and distended abdomen. These lateral depressions of the chest are in such a position that they are comfortably filled by the flexed forearms of the child, but it is improbable that the pressure of the arms has anything to do with their production. According to Stone,[39] flattening of the sides of the chest is less common than the formation of a transverse groove and occurs in about a quarter of the cases. The enlargement of the costochondral junctions, which forms the rachitic rosary, is often so great as to be plainly visible.

Pigeon Breast, Pigeon Chest, Chicken Breast, Keeled Chest, Pectus Carinatum.—The submammary flattening, the formation of a transverse sulcus, the flattening of the sides of the chest, and the flattening of the upper anterior chest enter into the formation of pigeon breast, which is simply the final outcome of a process of which the flattening in the first stage (Stone). In pigeon chest the sternum, and especially its lower part, is prominent, and the costal cartilages slope away abruptly at the sides. The anteroposterior diameter of the chest is increased, the lateral diminished, and the chest is much narrowed in front; it is also shorter than normal.

The reverse condition with a depression over the sternum may occur as the result of rickets. Both these deformities may be more pronounced on one side. These rickety chests are not only misshapen, but after the subsidence of the rickets they may remain unduly rigid and dwarfed.

Besides impeding respiratory movements, these rachitic chest deformities cause very little trouble, and when fully developed are practically incurable. Amelioration may sometimes be obtained by respiratory and general exercises. During the stage of development the treatment of the rickets is very important.

Similar conditions are sometimes due to obstruction of the air passages by adenoids, swollen turbinates, enlarged tonsils, polypi, or hypertrophic rhinitis. Tubby[40] relates several such cases, giving illustrations of the deformities produced. He says the proof of the dependence of the chest deformities upon the conditions named is given by their rapid improvement after the removal of the obstruction to repiration. A mild grade of these conditions is not uncommon in school-children, and is often accompanied by mouth breathing, and by inattention and apparent mental dulness, which clears up when the cause is corrected.

Chest Deformities Due to Lacing.—Certain chest deformities are due to pressure from without, and of these the commonest is the constriction of the waist and lower chest by corsets among civilized women. The use of corsets, even when loosely laced, prevents the proper expansion of the lower ribs in respiration, and forces the breathing into the upper thorax. This effect has been so universal that the exaggerated upper thoracic breathing of women is usually described as a normal peculiarity of the sex, but it has been pretty well established that boys and girls breathe alike until the girls put on corsets, and that women who do not wear corsets breathe very much like men, that is, with a bellows action of the whole chest, and not with a piston action of part of it. The evil effects of this abnormal constriction are seen not only in respiration, but even more in the crowding and displacement of the viscera. The liver may be deeply indented with the marks of the compressing ribs, and the ribs themselves are often misshapen about the waist. According to Dickinson and Truslow,[62] whenever one observes in unclothed women the angle between the cartilages of the rib at the upper part of the abdomen which approximates that of the male it is safe to guess that the individual is a singer. The stomach, intestines, and pelvic organs are frequently displaced downward, with many resulting ills. The rigidity and compression of the stays weaken the waist, back, and abdominal muscles, and interfere with the natural support and normal mobility.

The pressure of a back brace or frame often flattens the chest posteriorly.

Cobbler's Chest.—Some occupations cause special chest deformities, such as the cobbler's chest, due to the pressure of the last against the end of the sternum, producing a depression similar to funnel chest, but lower.

Tailors who sew in a bent-over attitude often have a hollow chest.

Deformities Due to Changes in the Thoracic and Abdominal Contents.—The last division of chest deformities includes those that are due to changes in the thoracic or abdominal contents.

The Inflated, Distended, or Emphysematous Thorax.—The typical chest of emphysema is large and

rounded or barrel-shaped. It is, in fact, a chest which permanently retains the shape of extreme inspiration, owing to the ballooning of the enlarged and dilated lungs, or, according to Campbell,[41] to overaction of the inspiratory muscles, the antagonistic pulmonary elasticity being impaired. The increased rigidity of the costal cartilages, which Freund believes to be causative of emphysema, Sumita regards as a sign or result of presenility. The ribs are strong and leave the sternum nearly at a right angle, making the thorax appear short. The sternum is prominent, especially at the angle of Louis, and the epigastric angle is large. The supraclavicular depressions are shallow or effaced; they may even be converted into elevations, if the pulmonary apices are markedly emphysematous. This is by no means always the case; they may even be deepened. The chest is immobile, and the breathing abdominal. While one may safely infer the presence of emphysema from the rigid, inflated chest, one should not call the large, deep chest of well-built and active men emphysematous, nor should one forget that in many cases of emphysema the lungs are not enlarged, and the chest fails to present the above-described characteristics.

One-sided distention of the chest, particularly in its lower part, may occur in pleuritic effusion and empyema of one side, in which conditions there may be bulging of the lower intercostal spaces. In proportion as the breathing is crippled on the affected side, there will be inflation and overaction of the well side, especially at the upper part in front. Hypertrophy of the heart, pericardial effusion, and aneurysm may cause enlargement in the precordial region, and marked enlargement of the liver or spleen may cause a bulging of the ribs on the corresponding side. Chronic distention of the stomach and bowels may cause prominence of the lower ribs on both sides. Effusions and enlargements of the internal organs will affect the shape of the chest in proportion to its flexibility. These deformities are therefore most marked in children, less in adults, and least often observed in the aged. In individuals with rigid chests changes in the internal organs may produce but slight effect.

The Phthisical, Phthinoid, Alar, Paralytic, or Rudimentary Chest.—This is partly a rudimentary and partly an atrophied chest. It has usually been described as flat or flattened, but Hutchinson[42] has shown that it may be not only relatively but absolutely longer, narrower, deeper, and rounder than normal, approximating the quadrupedal type. It is apparently a chest whose evolution has been arrested at a lower stage. In the chest of phthisis the ribs are depressed, and the intercostal and supraclavicular spaces may be sunken. The epigastric angle is diminished; costal breathing is lessened on the affected side.

Freund[53] regards an abnormal shortness of the first rib and a sheath-like ossification of its cartilage as a predisposing cause of phthisis, but Sumita[54] considers them the result rather than the cause of this condition.

If chest development is arrested in childhood or adolescence, the liability to phthisis is increased, and one may infer a certain predisposition to pulmonary tuberculosis from the existence of this chest in the young. The investigations of Gabrilowitch[43] confirm these views. He found that the ratio of the circumference of the best-shaped chest to the total height was as 1 to 1.6. The ratio of the mean anteroposterior diameter to the transverse was as 0.70 to 1 in normal individuals, but in phthisical individuals the proportion was 0.73 to 1. Rothschild[44] criticises Gabrilowitch's methods and conclusions, and gives the ratio of chest depth to chest breadth as 1 to 1.8 in healthy individuals, and as 1 to 1.5 in phthisical subjects with thorax paralyticus. He gives the chest circumference as one-half the total height, and the length of the sternum as one-fifth the chest circumference in the healthy, less in thorax paralyticus. He also states that the angle of Louis and the angular movement of the sternum in respiration are less in phthisis (see measurements by De Giovanni[45]). The whole subject apparently requires more exact and extensive study.

During the destruction of lung tissue atrophy of the muscles of the chest takes place, and is most pronounced on the side most seriously involved, and unilateral if the disease is unilateral.

Carcasonne[46] finds that atrophy of the scapulothoracic muscles takes place early and independently of general emaciation; it may even precede auscultatory signs. This atrophy is not accompanied by functional changes in the muscles, nor is their electric excitability altered; it advances with the progress of the pulmonary lesion, and is of considerable diagnostic value. The analogy of this concomitant atrophy of the muscles of related areas with the primary atrophy in joint disease is evident. In the latter case, however, the tonus and mechanical and electric excitability are said to be increased.

The very great importance of an active out-of-door life, of exercise stimulating deep breathing, and of free use of the arm and shoulder muscles for the round-shouldered and alar-chested, is apparent. Swimming, running, climbing, and throwing are particularly indicated.

Unilateral shrinking of the chest occurs in phthisis of one side. The deepening of one supraclavicular fossa is an evil symptom. Over a shrunken cavity the chest may present a depressed appearance, with hollow intercostal spaces. From the atrophy already mentioned, as well as from the traction of adhesions, there may be depression of the chest wall without cavity. After pleurisy and empyema, if the lung does not expand, the affected side of the chest may become markedly shrunken, and the whole thorax deformed with a scoliosis, whose convexity is toward the well side.

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Chest, Physical Examination.—See *Diagnosis, Physical.*

Chestnut.—See *Castanea.*

Chewstick.—The stems of *Gouania domingensis* L. (fam. *Rhamnaceæ*). This is a beautiful woody climber, growing both wild and cultivated in the West Indies, and other parts of tropical America, whose stems are used there as tooth-brush and powder combined. These stems are very tough and fibrous, and when cut in shortish pieces the ends are chewed until a rude, stiff brush is formed, with which the teeth are rubbed; a pleasant saponaceous froth of an aromatic bitter taste is formed in the operation, and the teeth are said to be whitened and the gums hardened by it. A tincture and powder are proposed as dental remedies. Internally, it acts as a mild aromatic bitter, and is used in its home as a constituent of small beers. Manufacturing houses offer a fluid extract, the dose of which is fl. ʒ i.–ij. (4.0–8.0). HENRY H. RUSBY.

Cheyletidæ.—A subfamily of the family *Thrombidiidæ* among the mites. The body is fleshy and transparent, and the enormous pedipalpi are formidable weapons for attack. *Chelytus* is the principal genus, and the curious genus *Syringophylus* parasitic in the interior of birds' feathers appears to belong here. See *Arachnida.* A. S. P.

Cheyne, John.—Born February 3, 1777, in Leith, of a family of physicians, his father, uncle, and maternal grandfather being medical practitioners. At the age of fifteen years he began to attend medical lectures at the University of Edinburgh, and obtained his medical degree in 1795, when he was but eighteen years old. After graduation he served in the medical corps of the British Army for several years and was placed in charge of the Ordnance Hospital at Leith in 1799. In 1809, having resigned from the army, he removed to Dublin, where he had a severe struggle with poverty for several years but finally was appointed physician to the Meath Hospital and soon thereafter was given the newly created chair of the practice of physic at the College of Surgeons. He now prospered and for twenty years had a very extensive practice, enjoying the large income for that time of from £1,500 to £2,000. In 1831, his health failing, he retired from practice and on January 31, 1836, he died.

Cheyne was an earnest student of medicine and an acute observer. In his work on "Cases of Apoplexy and Lethargy, with Observations on the Comatose

FIG. 1365.—John Cheyne,

Diseases," London, 1812, he described a peculiar change in the respiratory rhythm, noted also at a later period by Stokes, known as the Cheyne-Stokes respiration. Among the other works published by him are: "Essays on the Diseases of Children," in two volumes, Edinburgh, 1801–08; "An Essay on Hydrocephalus Acutus, or Dropsy in the Brain," Edinburgh, 1808; and "Pathology of the Membranes of the Larnyx and Bronchia," Edinburgh, 1809.

T. L. S.

Cheyne-Stokes Respiration.—A type of respiration in which the inspirations slowly increase in depth, reaching a maximum at the eighth or tenth, whereupon a corresponding diminution occurs up to complete cessation. Then after from five to thirty seconds of arrest, inspiration again begins and the cycle is repeated. This phenomenon, which had been seen by John Hunter, was made known to the medical profession by two professors of medicine in the Royal College of Surgeons, Dublin; Cheyne having described one case in 1816, while Stokes in 1854 described the phenomenon as a symptom perhaps pathognomonic of fatty heart. It is of interest to note that Professor James Little, a successor of Cheyne and Stokes, writing in 1911 makes the following statement (*Dublin Journal of Medical Sciences,* vol. cxxxi.). "I fear all we know about Cheyne-Stokes breathing is that it is a very striking phenomenon, not often seen, and seldom seen until the close of life." This statement should render superfluous in this connection any detailed account of the incidence of the phenomenon. In addition to fatty heart the symptom has been seen in arteriosclerosis, uremia, and various uncomplicated intracranial conditions. The cardiac component is very puzzling in character, fo while on the one hand the phenomenon occurs when the muscular fibers of the ventricles have almost disappeared, as in fatty heart, it is also observed in the very opposite state of ventricular hypertrophy, such as occurs in arteriosclerosis and advanced nephritis. The cerebral component is apparent in another series of conditions, to wit, uremia, apoplexy, cerebral congestion, tuberculous meningitis, and sunstroke. The so-called modified or mitigated form of Cheyne-Stokes breathing, characterized by the absence of an apneic interval, is not uncommon and appears to show merely a want of synergism between the circulation and respiration. Naturally of vital interest to the practitioner are the individuals in

whom the phenomenon, even when typical, possesses no necessary pathological significance. These comprise sleeping infants, healthy old men and certain cases of cerebral hemorrhage. Savill mentions a case of pontine hemorrhage in which the phenomenon had no prognostic significance. E. P.

Chicago.—A city of 2,185,283 inhabitants, situated upon the west shore of Lake Michigan. Its climate, although a very variable one and subject to sudden changes, with excessive heat or cold and increased humidity, is not an unwholesome one; and the death rate from consumption along the west shore of the lake is less than farther inland. According to Dr. John A. Robinson (*North American Practitioner*, Chicago, 1897, ix., pp. 296–298, "Chicago as a Health Resort") the physiological effect of the lake climate is to promote physical activity and mental vigor, and to increase bodily nutrition. "Persons," he says, "who have been predisposed to pulmonary tuberculosis have enjoyed robust health in this climate so long as they have avoided its bad features and observed other precautions." The favorable features of the climate, as Dr. Robinson gives them, are: first, air in motion, the winds sweeping down into the dark corners of the streets and alleys, and whirling the filth into the highways where the rain and sunshine disinfect it; these winds act as great atmospheric purifiers. Second, the lake purifies the air as it blows from its surface toward the land. Third, the large amount of sunshine. "Observations for several years," continues Dr. Robinson, "prove that the monthly mean of cloudy days is about ten a month; which means that the sunshine is present about two-thirds of the time." From the accompanying climatic table it will be seen also that the number of clear and fair days is two hundred and fifty-seven a year.

Climate of Chicago, Ill.—Latitude, 41° 52′; Longitude, 87° 38′. Period of Observation, Thirteen Years.

Data.	January.	April.	July.	Year.
Temperature (Fahr.)—				
Average or normal	25.8°	45.4°	72.3°	48.8°
Average daily range	14.9	14.3	14.3	
Mean of warmest	32.6	54	80.1	
Mean of coldest	17.7	39.7	65.8	
Highest or maximum	65	83	99	
Lowest or minimum	−20	17	50	
Humidity—				
Average or relative	76%	66.5%	70.6%	70.8%
Precipitation—				
Average rainfall in inches	2.04	3.65	3.96	37.58
Wind—				
Prevailing direction	S.W.	N.	S.W.	S.W.
Average hourly velocity in miles.	9	9.5	7.1	8.4
Weather—				
Average number of clear days.	7.8	8.1	12.9	108.5
Average number of fair days.	12.9	12.2	12.5	148.6
Average number of clear and fair days.	20.7	20.3	25.4	257.1

The authority above quoted does not think the Chicago climate contraindicates the establishment of a sanatorium, in the vicinity, for the treatment of curable cases of consumption. "At any rate," he says, "the climate in the lake region affords as good an opportunity as the climates of England and New England." For a statistical account of the Chicago climate one is referred to "The Climate of Chicago," by Professor Hazen, 1893, of the Weather Bureau, published by the United States Government.

Edward O. Otis.

Chickenpox.—(*Synonyms:* Varicella, Crystalli, Swinepox.) Chickenpox is an acute, specific, infectious disease characterized by successive crops of vesicles distributed over the surface of the body, which disappear, in from four to seven days, by desiccation. It is the mildest and least important of the eruptive fevers.

The belief, formerly generally entertained by the profession, that varicella is not an independent affection but a modified variola is now abandoned, save by a few clinicians who accept the teaching of Hebra and his followers. The differentiation was not generally accepted until after the smallpox epidemic in Germany in 1870–73. The proof of the non-identity of the two diseases is overwhelming.

Varicella, like the other members of the exanthematic group, is due to a specific virus, or poison, the nature of which is unknown. It is pre-eminently a disease of early life. It affects babes at the breast, attains its maximum frequency about the fifth year, and is rarely met with after the tenth year of age. It rarely occurs a second time in the same individual. Adults seem to have special immunity from the disease, even when unprotected by an attack in childhood. This is true of many infectious diseases, but the prevalent belief that varicella is a rare disease in adult life is erroneous and has led to many mistaken diagnoses.

Sporadic cases of chickenpox are observed, but it usually prevails as an epidemic. It is highly contagious, and few children who are susceptible to its influence escape when exposed. The mode of infection is unknown. The weight of evidence is strongly against its transmission by inoculation of the contents of the vesicles, though Steiner claims to have been successful in two cases. Holt locates the contagium in the vesicles. In a recent epidemic in a native prison in the Philippine Islands, which came under the observation of Dr. Tyzzer, repeated inoculations of the contents of both clear and clouded vesicles were made with negative results. The period of incubation of chickenpox is very variable and is usually given as from ten to fourteen days. Some authors give even a wider range. The incubation stage is without symptoms.

Symptoms.—Prodromal symptoms are not infrequently wholly absent, the appearance of the eruption giving the first indication that the child is ailing. When present, they rarely last longer than twenty-four hours, and are such as usher in mild febrile attacks, namely, anorexia, lassitude, general bodily discomfort, chilliness, and slight elevation of temperature.

The initial fever is mild, seldom measuring more than 101° F., and the constitutional disturbances are correspondingly slight, but in exceptional cases they may be as severe as those which commonly attend mild attacks of the other eruptive diseases. The eruption follows promptly on the first increase in temperature, and in a few hours attains its full development. Small hyperemic patches resembling roseola spots first appear and are speedily followed by vesicles. When fully formed, the eruption consists of perfectly transparent vesicles, more or less abundantly scattered over the body, globular or ovoid in form, and varying in size from a pinhead to a split pea, or even larger. They are unicellular in structure, collapse when pricked, and leave behind no swelling or elevation of the skin. A distinct areola may or may not be present.

The wall of the vesicle, formed by the outer layer of the epidermis, is very thin and easily broken.

When the eruption is abundant the body, as well described by Dr. Gregory, presents the appearance of having been exposed to a momentary shower of boiling water, each drop of which has produced a small blister.

The eruption appears first upon the trunk, and spreads irregularly over the entire body. It is most abundant upon the back and breast, and least so upon the face, where it is usually limited to the forehead. The scalp nearly always exhibits a full crop of eruptions, which, protected by the hair, maintains its physical integrity longer than in any other location, and thus renders valuable aid in diagnosis. The eruption is never confluent.

The occurrence of two, three, or more successive crops of eruption, each running an independent course, constitutes a striking and unique feature of varicella. Between the vesicles first formed new roseola spots appear, and soon ripen into fully developed vesicles. Thus, newly formed vesicles may be seen side by side with others in all stages of development, even to advanced desiccation. The irregularity in the course and development of the eruption is an important point in the diagnosis of the disease.

The varieties of chickenpox described by authors under the names of *Varicella lenticularis*, *Varicella conoides*, and *Varicella globata*, based on the various shapes assumed by the eruption, may be wholly ignored, since in every well-marked case vesicles answering all of these descriptions are abundantly found. In fact this variability in size and form of the typical varicellar eruption is a characteristic feature of the disease.

The mucous membranes are often implicated. The tongue, buccal membrane, and the mucous surfaces of the genital organs, especially in girls, are occasional sites for the formation of vesicles. In these locations the vesicles soon lose their epithelial covering, and leave small, round, superficial ulcers resembling the ulcers of herpetic stomatitis.

If unbroken by accident or by the scratching of the child to relieve the itching so generally present, the vesicles remain until the third day without change, when their contents become cloudy and desiccation begins.

At this stage a few scattered pustules may be observed, but these are purely accidental and not essential features of the disease. The vesicles begin to dry up in the center and form thin, brownish-yellow crusts, which soon become detached. Faint red spots remain, which pass away in a few days, and carry with them every trace of the eruption, but exceptionally depressed, slightly pitted cicatrices permanently mark the seat of a few of the vesicles. According to Osler ("Practice," 1912) cicatrices after chickenpox are more common than after varioloid.

Mr. Hutchinson has called attention to the gangrenous ulcers which sometimes, though rarely, complicate chickenpox in feeble, ill-nourished infants. In these cases a greater or lesser number of vesicles, instead of pursuing the ordinary benign course, become gangrenous, increase in size, and form black scabs of one-half to one inch in diameter, surrounded by dusky red areolæ. The ulcers heal slowly. In fact this condition may result fatally in infants whose constitutions are depraved by inherited taints or bad surroundings. Knowles (*N .Y. Med. Journ.*, May, 1911) has reported a case of hemorrhagic varicella in which there was also gangrene and has collated the recent literature.

Erysipelas is a serious, though rare complication. Holt has met with fatal cases. Synovitis and arthritis have been noted. Rare cases of fatal streptococcic or staphylococcic infections have been recorded.

Henoch and others have reported cases of nephritis occurring both as complications and as sequels. Varicella is not infrequently complicated by other infectious fevers. The combination of scarlatina and varicella has been often observed.

Diagnosis.—Varicella derives its chief importance from the liability of inexperienced or careless diagnosticians to mistake it for smallpox, or *vice versa*.

In variola, or well-marked varioloid, the physiognomy is so distinctive as almost to preclude the possibility of error. But in exceptional cases of varioloid the constitutional symptoms are so mild and the eruption so rudimentary and irregular that a careless examination will not suffice to distinguish them from the graver forms of varicella.

For two years or more an unusually mild form of variola has prevailed extensively throughout the country, especially in the South and middle West. The mortality has been almost *nil*. During most of the time varicella has been epidemic in a part of the same territory, which with the exceedingly mild type of variola has given rise to much confusion and many mistakes in diagnosis. Time will always clear up the diagnosis, but in the meanwhile the reputation of the physician and the safety of the community may be seriously compromised.

The absence of prodromal manifestations, the short initial fever, the rapidity and irregularity with which the eruption spreads over the body, the globular, nonumbilicated, transparent, unicellular vesicles, the absence of a distinct pustular stage, and the successive crops of eruption, which show roseola spots, vesicles, and crusts in close proximity, will rarely give room to hesitate in the presence of chickenpox.

While any case of varicella may present an occasional vesicle slightly umbilicated or with purulent contents, due to scratching of the child or accidental causes, the fact that this appearance is exhibited only by a few scattered vesicles, and is not the predominating character of the eruption, will suffice to establish the diagnosis.

It is well to bear in mind that a vesicular eruption which occurs in a child over ten or twelve years of age, especially if unvaccinated, or in an adult, is open to grave suspicion. The writer cannot, however, agree with those authors, by no means few in number, who maintain that varicella never occurs in the adult. He can recall several recent cases in adults which have come under observation.

The prognosis is wholly favorable. The danger, if any, comes from the rarer sequelæ or complications, of which nephritis is most to be feared.

Treatment.—Varicella is a self-limited disease and needs care rather than treatment. Light diet, cooling drinks, a gentle aperient, and confinement to bed during the febrile stage is all that ordinarily will be required. The intense itching is often most annoying and should be allayed by ordinary lotions. The hands should be kept clean and the nails closely cut so as to lessen the danger of infection from scratching the vesicles.

To prevent spread of the disease isolation should be maintained until the crusts have fallen, however. The matter of isolation should be decided for each case according to conditions. Since an attack very certainly renders one immune for life, it is often better to get through with the disease in childhood than to run the risk of contracting it in adult life under perhaps unfavorable and annoying circumstances.

W. J. Conklin.

Chicory.—*Cichorium.* The root of *Cichorium intybus* L. (fam. *Cichoriaceæ*). A perennial, milky-juiced, European herb, with dandelion-like leaves and tall, sparsely branching stems, bearing large, delicate, bright blue flowerheads. It is very abundantly naturalized in this country, along roadsides, and is also extensively cultivated both here and abroad. The root is fleshy and branched, very much like that of dandelion when dry, but rather larger, and deficient in regard to the bright yellow woody center so distinctly seen in the cross-section of dandelion. It is grayish brown externally, whitish within, generally odorless, and but slightly bitter. The cultivated root is larger

and darker than the wild. It occurs in commerce mostly cut into halves and quarters of transverse sections, and is heavily wrinkled in drying. The leaves, which are somewhat employed as a salad, are irregularly pinnatified, with a large terminal and small lateral segments. They resemble lettuce in taste, but are more bitter.

The roasted root is very extensively used as an adulterant of, or addition to, or substitute for, coffee, and this use is steadily increasing. In some European countries, especially England, it is generally assumed that the customer desires the addition of chicory unless he directs otherwise. To the natural taste, it imparts a bitter and nauseous flavor to the beverage, but this, by custom, becomes tolerable or even agreeable.

Chicory is scarcely entitled to rank as a medicine, although it is laxative and about similar to dandelion in its effects. The root contains *inulin*, like many others in the family, *bitter extractive*, and *sugar*. The flowers contain a peculiar glucoside.

HENRY H. RUSBY.

Chigger.—Chigoe, jigger, the sand flea, *Sarcopsylla penetrans*. The female of this species buries the anterior portion of her body in the flesh of man and her abdomen becomes enlarged; she then discharges a number of eggs. This species is a great pest in some regions. In one reported case a man had three hundred on his body. See *Insects, parasitic*.

A. S. P.

Chilbain.—See *Dermatitis Calorica*.

Childhood.—Only in very recent years has the child begun to come into its own; the raising of plants of many kinds and of brute animals has for many centuries been a scientific art, but only now are we beginning to realize effectively that "children are the most important of all crops." Childhood is still, however, comparatively little understood save in the most obvious respects, and there yet remain to be written really scientific treatises on the nature of the child, physiological in particular, properly adequate to the unique importance of the subject.

The fourteen years or so between birth and puberty we may, although not technically, know as childhood. Its beginning is the separation, for the most part, of the new individual from its mother's body. Its other terminus is the commencement of the time when this new being may, in turn, become mother or father to another generation. In most all respects childhood merges into adulthood gradually. It is only in the reproductive phases of mental and bodily function that entirely new events begin, although these widely pervade in one way or another both the body and the mind.

The commencement of childhood is likewise gradual in some respects so far as the various bodily functions go. Yet the unique act of being born, the beginning of respiration, of digestion, of excretion, the changes in the circulation, and the starting of action in most of the sense organs, make the extrauterine life sufficiently different from that within the womb. Formerly the fetus was influenced from without itself almost wholly (aside from mechanical impacts wholly) through the mother's blood. Now, however, it begins a much more varied career and becomes more nearly unified with its environment through many various channels and in a large number of respects. As Fiske long ago pointed out, it is because of man's uniquely long childhood more than anything else that his general predominance in the world is due: meanwhile he imitates his parents.

Growth has been the laborious subject-matter of many researches since E. Hitchcock's work and that of Henry Pickering Bowditch on Boston school-children in 1878. Of late more attention has been paid to growth in relation to exercise and to sex, and especially to mental growth. H. Vierordt's "Daten und Tabellen" remains the chief reference-book on the statistics of children's growth as in other organic fields.

Weight.—The average weight at birth of the female child of American parents is about 3,150 grams, or seven pounds, and that of the male child is one or two hundred grams more. Largely for the reason that the average infant assimilates little nourishing food for the first day or so, its weight falls in two or four days 175 grams and often more. In babies fed from vigorous breasts, however, this loss is often much less or even none. At ten days of age the child weighs 100 grams more than at birth. For the first six months, speaking roundly, the infant gains twenty-five grams daily, and for the next six months fifteen grams. The birth-weight is about doubled at five months and trebled at fifteen months. When a year old the child weighs 9,000 or 9,800 grams (20–21 pounds), and this weight is doubled at seven years and quadrupled at fourteen. Breast-fed babies gain in weight much more regularly and certainly during the first half-year, but later the difference between these and those fed from the bottle with modified cow's milk is not so marked. The liability to death is very much greater in bottle-fed infants, especially if the milk be improperly modified and cared for, and the improvement in infant mortality-rate in most localities in the last five years, since this matter has been properly attended to by education, is most gratifying and should encourage the medical profession to be energetic in other needed reforms—for the reward is great.

Data compiled by Burk from measurements made by Bowditch and others in Boston, St. Louis, and Milwaukee (68,000 children) give the weight-norms in kilograms for American city-children as follows:

Approx. age.	6.5	7.5	8.5	9.5	10.5	11.5	12.5	13.5	14.5	15.5	16.5	17.5
Boys	20.50	22.45	24.72	27.03	29.66	32.07	34.88	38.46	43.18	48.72	54.88	
Girls	19.69	21.64	23.81	26.03	28.53	31.52	35.70	40.23	44.59	48.40	50.94	52.34

Whipple in his valuable "Manual of Mental and Physical Tests" (Baltimore, 1910) reports general results as follows in part from the weight data already available: As in case of height, girls exhibit the prepubertal increase in weight some two years earlier than boys, and are for the years twelve to fifteen heavier than boys of the same age. Growth in weight, as in height, is subject to some lessening of rate at nine years for girls and at eleven for boys. Boys continue to increase in weight after girls have practically attained their maximal normal weight. Girls grow most rapidly from ten to fifteen years, boys from twelve to seventeen years. Mean variations in weight are largest during the period of fastest growth. First-born children exceed later-born children in weight at least during the period from six to fifteen years, though the reverse is true of weight at birth. The difference is slight but very regular (Boas). *Children of the non-laboring classes are as a group*

heavier than children of the laboring classes (Bowditch). Children of American-born parents are heavier than those of foreign-born parents. The boys in truant schools are lighter than boys in the public schools save at the age of ten (Kline, Smedley). Children with abnormalities are below the average in weight (MacDonald).

It is full time that physicians began to realize that the average child of the "laboring" classes (the term is wholly misleading unless we remember as we use it that it refers to muscular rather than to mental or psychophysical labor) is somewhat, and often greatly, *underfed*. Knowledge of this fact by the medical profession will sooner or later lead to reform. Fundamental evidence of the truth of this deplorable proposition is to be had from the extensive work of Bowditch quoted above and printed in italics. More direct confirmation was offered lately by E. A. Locke of Boston, in a paper before the American School Hygiene Association in that city. Eighty-two per cent. of the 191 children whose home diets were studied were between the ages of eight and fourteen and they were all tuberculous in one place or another; sixty-six per cent. were in the first stage of the disease.

"The investigation of the home diet referred to above revealed an almost uniform deficiency in the amount of nutriment furnished the children, and in a considerable percentage of instances, obvious faults in the selection and preparation of the food. An excellent idea of the character of the diet provided by the family as compared with the total ingested is given by the following table.

Case No.	Wt. Lbs.	Protein (Grams)		Carbohydrate (Grams)		Fat (Grams)		Calories		Total Calories
		School	Home	School	Home	School	Home	School	Home	
307	78	66	26	230	70	54	21	1,716	589	2,305
5630	68	76	14	226	54	71	16	1,899	428	2,327
5236	59	131	26	344	55	49	14	2,403	421	2,824
6704	52	45	20	162	94	42	20	1,239	653	1,892
5543	59	68	21	300	50	58	23	2,048	505	2,553
		56	22	239	81	54	23	1,712	636	2,348
1315	70	38	40	216	114	55	40	1,553	1,003	2,556
3564	102	80	30	298	85	81	37	2,303	816	3,119
4770	82	80	14	265	79	62	17	1,991	539	2,530
5020		84	27	350	66	71	27	2,440	632	3,072
1418	86	90	25	249	101	65	17	1,994	675	2,669
5571		65	34	329	161	61	25	2,182	1,033	3,215
6102		86	16	301	70	71	19	2,247	529	2,776
4758	78	73	20	292	88	57	31	2,027	731	2.758
6127	56	83	38	300	112	71	31	2,230	993	3,133
6164	60	77	33	272	90	63	32	1,917	802	2,719
2771	70	80	29	434	96	69	29	2,749	782	3,531
2144	42	55	22	198	89	46	25	1,465	688	2,153
900	102	115	67	340	79	125	46	3,028	1,107	4,135
2472	100	127	89	352	77	148	58	3,340	1,220	4,560
6062	110	83	23	319	78	98	25	2,559	647	3,206
4683	114	75	12	248	28	53	15	1,817	304	2,121
3604	94	71	22	314	71	76	22	2,286	586	2,872
1194		90	28	299	65	71	35	2,243	719	2,962
Home		95	24	323	82	77	27	2,430	686	3,116

Considering the fact that the children were supposed to have a full meal at home before leaving for the hospital school in the morning and on their return at night, the home diet is surprisingly deficient. The uniformity in the fuel value is also striking. It will be seen that the minimum total calories provided was 304 (case No. 4683) and the maximum 1,220 (case No. 2472) and the average 705 calories. An examination of the grams of each food constituent in the home diet indicates that all participate in the deficiency but the carbohydrate to a proportionately greater degree, however, than either the protein or fat. The average amount of carbohydrates was but eighty-one, the protein twenty-five, and the fat twenty-seven grams. In one instance (case No. 4683) the protein was only twelve grams and in the same case the carbohydrates twenty-eight grams. It will be seen that the average number of calories yielded by the school diet was 2,153 while that by the home diet was but 705, or a ratio of nearly three to one."

The total food taken is shown in another way in the following table:

Weight in kilograms.	Av. No. of calories per kilo. of body-weight.
17 to 19 (5 cases)	137.4
20 to 24 (7 cases)	112.5
25 to 29 (12 cases)	103.8
30 to 34 (4 cases)	99.7
35 to 39 (2 cases)	78.6
40 to 45 (4 cases)	73.8
55 (1 case)	67.4

These amounts are from 50 per cent. to 100 per cent. higher than the food-requirement standards as given by Camerer. No forced feeding was done and close observation daily failed to show any sign whatever of overfeeding. "Our experience in the hospital school" says Locke, "leaves us with the conviction that in treating tuberculous children in open-air schoolrooms, especially during the winter months, a diet comprising from 90 to 120 grams protein, 300 to 400 grams carbohydrate, and 100 to 125 grams fat, or a value of 2,500 to 3,200 calories per diem" is necessary. To the physiologist, on the other hand, here is evidence enough, when added to that of the undergrowth of relatively indigent children (Bowditch), and to the results of general observation, to the frequency of tuberculous infection among them, etc., that such children are often if not usually underfed.

Height.—The average length of babies when born is 49 or 50 centimeters. In a year this has increased to about 70 centimeters, in two years to 79 centimeters, in three years to 86.5 centimeters, in four years to 93 centimeters, and at the end of five years the average height is almost a meter. After this period the child grows not far from 6 centimeters yearly, so

that when he or she is fifteen the height is just about treble that at birth, or 150 centimeters, its doubling having occurred at the beginning of the seventh year. Rotch notes that growth in height is fastest in the spring.

Heubner's table of statures during the first year, derived from various observers, is as follows:

	Boys.	Girls.
	cm.	cm.
At birth	51.0	49.0
End of the first month	52.5	51.3
End of the second month	55.3	54.8
End of the third month	57.8	56.7
End of the fourth month	60.1	58.7
End of the fifth month	61.3	60.2
End of the sixth month	62.6	61.5
End of the seventh month	64.6	63.2
End of the eighth month	65.6	64.3
End of the ninth month	67.8	65.4
End of the tenth month	[67.0]	67.2
End of the eleventh month	69.0	68.1
End of the twelfth month	70.3	69.2

The mean statures of children between the end of the first year and school age are lacking owing to the inaccessibility of large numbers of infants at this age. Heubner's figures for boys, however, seem to be fair means: at end of first year, 70.6 centimeters; second year, 81.1; third year, 87.2; fourth year, 92.5; fifth year, 99.9 (a boy on his fifth birthday "should be" in Germany a meter tall); end of sixth year, 106.5 centimeters.

The best figures available (because made by experts and from more than 88,000 American children) are thus arranged by Boas:

Age.	5.5	6.5	7.5	8.5	9.5	10.5	11.5	12.5	13.5	14.5	15.5	16.5	17.5	18.5
Boys	105.90	111.58	116.83	122.04	126.91	131.78	136.20	140.74	146.00	152.39	159.72	164.90	168.91	171.07
Girls	104.88	110.08	116.08	121.21	126.14	131.27	136.62	142.52	148.69	153.50	156.50	158.03	159.14	.....

Whipple reports the following important results among others from stature statistics so far gathered: There is a period of slower growth in height in boys at eleven years of age, and a similar, though less marked, retardation in girls at nine years of age. During the period of approximately eleven to fourteen years girls are taller than boys of the same age, because the prepubertal acceleration of growth occurs earlier in girls. Boys continue their growth in height later than do girls. Children of purely American descent are taller than those of foreign-born parentage (Bowditch, Peckham). *Children of the non-laboring classes are as a group taller than children of the laboring classes* (Bowditch, Roberts). According to Bowditch, large children make their most rapid growth at an earlier age than small ones, but according to Boas this induction is untenable. The height of American-born children is modified by density of population. Urban life decreases stature from five years of age (Peckham). According to Kline, boys in the public schools are taller than boys in truant schools, save at the age of ten. Similarly, Smedley found the boys in the Chicago School for Incorrigibles and Truants shorter than more nearly average boys from the tenth year on. Children with abnormalities are inferior in height to children in general (MacDonald).

Goddard has very recently published statistics from measurements made in nineteen institutions by as many observers which show that the feeble-minded are heavier at birth than are normal children, and that the growth of the defectives is much more erratic, earlier to stop, and less in the total than in normal children and adolescents.

Head-measurements are of importance in estimating the status of children for practical, as well as for scientific, purposes. Boas, West, Chamberlain, and other Americans have made such measurements extensively and these are thus tabulated by West

Diameters of the Skull and Cephalic Index.

Age.	Average length		Average width.		Cephalic index.	
	Boys.	Girls.	Boys.	Girls.	Boys.	Girls.
	mm.	mm.	mm.	mm.	per cent.	per cent.
5	176	174	140	138	79.56	79.40
6	177	172	142	139	78.94	79.60
7	179	175	142	140	79.42	80.02
8	180	174	143	141	78.71	80.41
9	181	176	144	140	79.63	79.41
10	182	177	145	142	80.30	79.46
11	183	180	144	142	78.80	78.90
12	183	180	145	143	79.40	79.40
13	184	181	147	145	79.50	79.60
14	187	183	147	144	78.60	79.00
15	188	184	148	146	78.59	78.99
16	191	184	149	144	77.81	78.48
17	189	185	150	146	78.34	78.50
18	192	186	151	147	78.88	79.36
19	192	183	150	145	78.33	79.68
20	195	182	152	147	77.88	79.41
21	192	186	153	145	79.29	78.36

Whipple notes the following considerations (among others) from these statistics: In boys, length of head continues to increase until the age of twenty-one; in girls, until eighteen. Growth both in length and width is very irregular. Boys' heads are longer and wider than those of girls throughout the whole period of growth, and consequently throughout life. Width of head is greater in precocious children than in dull children (Porter). Binet similarly finds the heads of the unintelligent are smaller than those of the intelligent in all dimensions save in vertical diameter and from base of nose to the end of the chin; where the contrast in intelligence is very great, differences averaging three or four millimeters appear particularly in the breadth: bright children have wide heads. MacDonald showed that dolicocephaly (long-headedness) increases as the ability decreases; dull and unruly boys are dolicocephalic. German (Munich) children of six and one-third years show results somewhat different from those last cited for American children. Miss Lee found no correlation between the estimated skull capacity and the intellectual capacity (what is "intellectual capacity"?) of sixty men and thirty women.

Theoretically more important than the norms of weight, stature, etc., are two related subjects that are just beginning to receive something of their due attention—namely, *physiological* (as contrasted with chronological) *age;* and the respective *variabilities in the appearance of developmental events.* The former has educational importance of the first degree and without knowledge of the latter the former is empirical rather than a matter of scientific determination. Neither Crampton's criterion of physiological age (pubescence) or Rotch's (the ossification of the

epiphyses) seems general enough to be an adequate index of a thing so extremely complex as physiological and psychological age; we might more reasonably seek it, it seems to the writer, in some such event as the rise or awareness of conscious personality as an agent, the "finding of one's self," appreciation of motor capability in general, conscious skill in the use of the neuromuscular mechanism—or however else this fairly definite milestone in personal evolution might best be denoted and described. One can readily see in the developing individual three general stages—namely, the vegetal, the "animal" (brute), and the properly human. True criterion of physiological age will be delimited only when someone has defined the definite characteristics of the beginning of the third stage. Perhaps the functions of the neuromuscular mechanism will most accurately provide the data for such a standard of comparison.

Franz Boas of Columbia has determined the variability of various structural and functional events, and we quote below a table of some of them. It is obvious that the variability in general is inversely as the rate of rejuvenation and more or less directly as the rate of senescence, to adopt and use Minot's terms. We may suppose, then, that in general variability depends, and largely perhaps on the rate of change or growth at that period.

"The mean square variability of the chronological age at which a certain point in the physiological development of an individual is reached is contained in the following table:

Age.	Observations.	Variability.
0.0	Pregnancy	± 0.04
0.6	First incisors	± 0.21
1.6	First molars	± 0.31
4.2	Ossification of scaphoid bone, girls	± 1.4
4.2	Ossification of trapezoid bone, girls	± 1.2
5.8	Ossification of scaphoid bone, boys	± 1.1
6.2	Ossification of trapezoid bone, boys	± 1.3
7.0	Inner permanent incisors, girls	± 1.6
7.5	Inner permanent incisors, boys	± 1.4
8.9	Outer permanent incisors, girls	± 2.1
9.0	Bicuspids, girls	± 2.8
9.5	Outer permanent incisors, boys	± 2.1
9.8	Bicuspids, boys	± 1.6
11.2	Permanent canines, boys	± 1.4
11.3	Permanent canines, girls	± 1.0
12.7	Beginning of pubescence, boys	± 1.6
12.8	Second molars, girls	± 1.6
13.2	Second molars, boys	± 2.0
14.6	Completed pubescence, boys	± 1.1
14.9	Puberty, girls	± 2.0
19.3	Wisdom teeth, boys	± 2.1
22.0	Wisdom teeth, girls	± 1.8
35.0	Preauricular wrinkles	± 6.6
36.5	Hair on tragus	± 8.3
44.5	Menopause	± 5.3
62.5	Death due to arterial diseases, men	±13.2

"It appears from this table, which may be represented in the form of a curve, that the variability of the physiological stages of development increases very rapidly—roughly speaking, so that its logarithm is about proportional to the actual age, or, to use the term applied by Dr. Crampton and Professor Rotch, to the "chronological age." The causes that lead to this rapidly increasing variability are so far entirely unknown. It is certain, however, that there must be definite causes at work which bring about this phenomenon; for, if the variability were due to accidental causes only, it would increase considerably slower than in a ratio proportional to the increasing age."

The proportions of the various organs differ not a little in childhood and adulthood. Of these the relative weights of *brain* and *spinal cord* to the body are most conspicuous. According to Bischoff, the brain at birth weighs one-eighth as much as does the whole body, at the end of one year one-sixteenth as much, and at fourteen one-twentieth as much. In the adult the brain is only about one-forty-third of the body by weight. Similarly with the spinal cord: at birth it is one five-hundredth as heavy as the body, but in the adult only one fifteen-hundredth as heavy. This relative preponderance of the nervous system is clearly seen in the conduct of the child. The actuating aspects of the nervous system are especially conspicuous, while its inhibitory functions are relatively little developed.

The *liver* and the *adrenals* are relatively large in childhood, the *spleen* relatively small.

The *blood* is relatively less abundant in new-born children (1 : 15.5) than in adults (1 : 13), as is also its hemoglobin, seventy-five per cent. On the other hand, the lymph is more abundant proportionally, as the more active metabolism of the child demands.

At birth, according to Schiff, the blood contains from seven to eight million erythrocytes (reds) per cubic millimeter, reaching its normal figure of four and a half or five million, however, in about a fortnight thereafter. Grendobin found the leucocytes (white cells) also more numerous soon after birth: from the tenth day to the end of the first year the number per millimeter varies between ten and fourteen thousand, while in older children the number ranges from seven to ten thousand. During the first year from three-quarters to two-thirds of the leucocytes are lymphocytes and only one-third polynuclears, while in the adult the proportions are just the opposite. The specific gravity of the blood in the first month is about 1050 (Hoch and Schlesinger), about eight thousandths less than the mean specific weight of adult blood. v. Dusch found that in the newly born the ratio of the *heart* to the body weight is at its maximum, that it sinks during the second year to a relative minimum, rising again up to the seventh year, after which (cf. the brain) the ratio remains constant, save for the life-minimum during the last year of puberty.

The *circulation* during childhood differs from that in adult life chiefly in its irregularity and variability. Especially is this so in girls and during the first six or eight years. This is due to several causes, among which are the greater elasticity and variability of the tissues, particularly the blood-vessels; the incomplete development of the circulation regulating nerve centers; and the greater irritability of the nerves. There is often a better marked dicrotism in the pulse of a child than can be found in adults. This is due doubtless to a greater elasticity of the arterioles. The *pulse-rate* appears to lessen from its beginning early in fetal life (up to about seventy years, when it increases slightly), and to be always faster in females than in males. As was said above, in the fetus it is from 160 down to 120 or so; at one year it is about 110; at four years 100 or more; at eight years 85; four years later 80; in adult years fron 70 to 80. For girls the rates are considerably higher. Many cases of heart-rate as low as 35 are to be found in every long series of pulse records. According to Vierordt the *circulation time* at birth is twelve seconds, while recent research has shown the time required in the adult to be about forty seconds. There is little satisfaction to be had clinically in the child's pulse because it is so variable a process even in perfect health, especially up to the ninth or tenth year.

Because of the more active muscular life and metabolism of the child, the *lymph flow* in children is livelier than in adults. The vital process is correspondingly strong. The lymph glands and the lymph vessels are relatively larger. Digestion (especially) of fats) and nutrition are relatively better in childhood, the lymph taking an important part in nutrition.

Respiration during childhood differs likewise from the adult process chiefly in its greater activity and in its larger variability under different circumstanc e s

The breath movements are more diaphragmatic and abdominal than in the adult, the intercostal muscles being relatively weak. The respiratory movements of the chest according to Uffelmann are at birth 35 per minute (up to 60); at one year old, 27; at two years, 25; at six years, 22, and at twelve years, 20. Very often indeed, however, one sees breath rates averaging five higher than these figures indicate. The breath rhythm is very vague during the first years of life and varies greatly from little causes, such, for example, as emotions, muscular activity, and physiological variations in body temperature. Periods of apnea of short duration are normal, while the rate on either side of such a period may vary many breaths per minute, at one time 70, at another 40. The imperfect connection of the various vital centers in the medulla plus the relative strength of the emotional expressions will in part explain these irregularities.

The depth of breathing (relative volume of air inspired) by infants has been determined by Gregor. He found the number of cubic centimeters of air inspired in sleep during the first semester to average 35, at the middle of the second year 78, and at the end of the latter, 136. In waking hours these figures are smaller. A child six months old breathes in about 2,500 c.c. per minute, and one eleven or twelve years of age about double that amount—three hundred liters per hour.

The bronchi and trachea are proportionally larger than in adulthood, while the alveoli are relatively smaller. Because partly of this we find the common pneumonia of infancy to be of the bronchial type, while that of middle life affects the alveoli more especially: lobar pneumonia.

Nutrition in children is, in general, more vigorous in all directions than it is in adults, excepting in the first few months. The full power of the digestive enzymes does not develop all at once, but more or less gradually in the first third or half of the first year. This is particularly true of the amylolytic juices. Starch, in particular, is ill-digested in the first months. Normally, that is in woman's milk, the only carbohydrate ingested is lactose or milk-sugar. In general, however, the child from three years onward digests more vigorously than the adult does, for the supply of digestive juices is proportionally greater and the alimentary movements more active. It is by this means that the child's commissary organs are able not only to replace the protoplasm worn out by the intense youthful activities, but to do more—to cause the rapid growth of the body. As we have seen, this causes a doubling of the body weight between seven and fourteen years. The child's digestive system, like all his others, is more plastic and more adaptable than the adult's, not having, as yet, become habituated to certain ruts such as most grown-up persons fall into, in part of mental origin but always in the nature of defect.

Gundobin found the *length of the intestine* of the nursling to be proportionally greater than that of the adult by about thirty-three per cent.; the small intestine is relatively longer than the large. In infants the entire intestine varied in length from 132 to 376 centimeters (as compared with 612 to 904 in the adult). The number and height of the valvulæ conniventes are less proportionally than in the adult; there averaged in five intestines examined a few weeks old between 200 and 400 of these (while the adult has from 600 to 850). On the other hand, the number of villi is greater in the infant—seventeen to twenty-six in a running millimeter of the jejunum to the adult's eight to sixteen. The glands of Lieberkühn are shorter than in the adult, but are thicker and more numerous; the solitary follicles are also more numerous and Peyer's patches larger. The musculature of the intestine of young children, and its nerves, are both undeveloped as compared with the same important organs in the adult.

Korowin found that the parotid gland began to secrete ptyalin only in the fourth week. Zweifel found the pepsin in the new-born stomach as efficient as in the adult, and recognized protein- and fat-splitting ferments in the pancreas. (Data quoted by Heubner.)

Muscular action in childhood is more lively but inherently less accurate than that of the adult. The ultimate usefulness of childhood lies in its ability to elaborate the neuromuscular mechanism into the wonderful perfection seen in the capable and clever adult. All know how vastly complex this machine is, how countless its coordinations and its combinations of movement. In the infant up to four months or so "voluntary" movements are of no immediate use at all, for they are so much at random and so grossly inexact as to be only general tendencies of action toward some object or end. From this, the merely formative stage of neuron interknitting, up to the expertness of the clever craftsman or performer in a thousand different ways, the development is in the direction of the acquirement of better and ever better and more numerous coordinations and motor adjustments. For this the new individual, philosophically speaking, was "carnalized"—to develop his personality in one way and another by satisfying *effort*, and always only by means of his neuromuscular mechanism, basis of his life, directly or otherwise.

At birth the outfit of the human animal is an impulsive one, because built principally out of protoplasm which has inherent in it the impulse to activity. This impulse determines action of some kind. In the second place, the efficient organism of the child at birth is inherently "reflex," the neuromuscular part of it being made up of a series of circuits and "reflexes" that includes, in the third place, a whole series of purely reflex inhibitions. The young infant has a well-defined set of these reflex inhibitions, as may immediately be seen from the phenomena of reflex attention manifested by adapted inhibitions to sensory stimuli of adequate kind. In the fourth place, the young infant at birth has a well-determined set of reflex innate desires dominated by dull pleasure and pain. In these four ways, at least, we can characterize the psychomotor outfit of the infant when he "comes into the world." We will find instances illustrating all these characteristics in the books on child study, and a moment's experimentation demonstrates them readily on the latest dear comer into our household. Such an impulsive and inhibitory reflex mechanism dominated by dull pleasure and pain contains, but latent and potential, the material out of which develops the motivated freedom which constitutes *humanity* free to do or not to do, and therein the only truly moral thing on earth, as Immanuel Kant has long since proclaimed.

About the actual stages of development of the different parts of the brain and cord in the child at birth there is still much unfortunate ignorance, so difficult is the practical problem of neurohistology. Already then, however, the cerebellum is more or less complete in general, we may suppose, because it is an afferent and efferent mechanical center carrying on mechanical coordinations. Again, the reflex apparatus of the cord, etc., is at birth fairly well finished. The mechanism of reflex inhibitions is more or less completed (we know but little as to its location unless it be in the cortex) and, sometimes, it seems as if reflex recognitions were more or less possible very early in the first year. In this suspected recognition we have a strongly psychical element, and a highly developed and complex thing—reflex recognition of the nursing bottle for instance, of its mother's face, and of other things very important to the child, such especially as the power of recognizing the difference between a smile and a frown. It would be difficult to suggest the brain paths for such functions as reflex

inhibition and recognition that did not involve widely separated portions of the cortex of the hemispheres, if not of the internal nuclei. However doubtful the neurology, the facts of occurrence at an early date allow, none the less, of no doubt at all. What seems especially needed is definite knowledge as to the relations of the cortex, the thalamus, and the medullary bulb at and soon after birth. When we have that we shall truly understand, it seems likely, such basally important human functions as recognition and inhibition —and not before.

A child three or four months old of course cannot make even the most simple voluntary movement. Show such an infant a big red rubber ball, and however much he wishes it, he cannot stretch out his hand to get it. He can and does, however, make general arm and leg movements, and this fact shows that there is ready communication of indefinite motor excitement through the central nervous system. It is not until the sixth or seventh month of life at least that the child begins to show capability of stretching out his hand deliberately toward an object. He cannot do it before, obviously because his "motor" neurons, the "centers," have not developed or have not interconnected, or both. The known physiological facts are corroborated by observations on infant behavior that lead us to believe that the neuronal lack in question is largely the connection, extensive and complex, between the rind of the hemispheres and the reflex vegetative mechanism of the sympathetic, the cord and bulb, and cerebellum.

The first step in the process of the personal evolution of voluntary movement, then, is probably an actual development in the extent and in the complexification especially of the cerebral neurons; the underlying development of voluntary movement is an anatomical one; an integration of the personal neurons above with the already elaborate system of vegetative, racial, neurons below. For the purpose of making things short and technical we may call this basal process "chemotactic neuronal integration." Now, in fact, we do not know much about chemotaxis, the movement of certain cells toward or from other cells under chemical attraction. The subject has been discussed chiefly in regard to the movement of plants and of protozoa. It is, at any rate, a growth or movement of protoplasm brought about by forces we call chemical. One finds an elaborate discussion of the subject in the writings of Max Verworn, for example. Ramón y Cajal, conceded to be one of the experts of the world upon this subject, and his opinions important because he has studied things in the light of the latest methods (including osmosis, etc.), supposes that the interknitting of the neurons occurs under some form of chemical reaction. The whole tendency of physiological causation being in this same direction, and no other theory even as satisfactory, we may tentatively accept the hypothesis as the cause or method of the early correlation of the neurons underlying the evolution of the individual as a free agent. As we have already seen, the cerebellum at birth, as the mechanical means of coordination, is much more complete than the cortex of the larger brain, so that we have to think of the growth at the basis of motor development as taking place more in the large brain than in the cerebellum during the early months of extrauterine developments, as well as later, and indeed throughout the life of the individual. The whole tendency at present, as Hemmeter has recently pointed out, is to unify chemotaxis in the nervous system with harmonic and perhaps with kolyonic action at the "synapses."

Much growth at the basis of deliberate motor development takes place also, there can be little doubt, in the large internal nuclei of the hemispheres.

Another factor in the process of the development of voluntary movements in the young infant is that of a gradual conscious clarification of the "motor ideas." Here come in again the impulse to activity as well as reflex action. In fact, from the earliest stages of intrauterine life, say at four or five months, every time the infant moves at all there are sensory impulses or, to speak more accurately, afferent impulses, sent to its brain, and the brain, as we know, is the chief organ of consciousness. Gradually, in the course of weeks and of months of kicking about and of general reflex activity, these sensory impulses which are continually being sent to the brain become clearer and plainer to "the organ of consciousness," if not to the actual focussed consciousness.

A third factor in the development of deliberate movement as a faculty in the infant, for lack of a better term, we may call the desire in each case to make the particular movement. This factor, always present in the young child and much more conspicuously than in the adult, is obviously a feeling, and an inherent part of the neural complex of the infant's behavior. It is a part of the innate interest and desire to have and to do things.

A fourth factor to consider in the process of the development of voluntary movement is a practical working knowledge of spatiality, of that which we call "space." The practical development of the concept of space in the infant's mind helps to develop its powers of voluntary movement. A child, for instance, would not reach out for the moon if it consciously realized that the moon were hundreds of thousands of miles away from its grasp. The child does things which the rational being fully informed would not attempt to do. This complex acquired sense of space is apparently one of the essential factors which help to develop the power of making voluntary movements, just as this phase of our elemental understanding of things depends for its existence in the mind on the tridimensional voluntary movements of the body.

The last factor of the development of voluntary movement that we need here specify is that which we may designate, but too elaborately, as self-confidence, always more or less important. At first in the infant this awareness is apparently an actual definition of a clear and a concise knowledge of the power to make one particular movement. The books detailing observations of child development (see, for example, the present author's "Moto-sensory Development," 1910, page 141) give instances that show beyond doubt that, except in movements properly classed as semi-voluntary or hereditary, this kind of cue is often necessary for the first performance of a new voluntary movement. With all the mechanism constructed and put together needful for a certain movement, still the movement may remain unperformed for lack of knowledge, certain and definite, that that particular movement is performable.

Such are some of the psychoneurological conditions that attract most conspicuously the attention of the physiologist observing infantile behavior. Without a doubt, these and other determinants are lively conscious experiences (the redundancy here is for emphasis) in the active states of the young baby. There is no one, not too old or too amnesic to hark far enough back, groping in the dim dawn of his memory, but who will recall that even at that late day of three or four years of age voluntary efforts were still matters of serious conscious import, although already the most frequently repeated movements had become by habituation easy and their underlying conditions, sometimes painfully conscious before, subconscious and dim to almost any extent. This is the process that goes on inevitably year by year and it marks at all stages of personal evolution the basal opposition between the reflex and the voluntary, between the mechanical and the

free, between the vegetative (or racial) and the personal or human.

Body temperature is another function of the child-organism which is characteristically variable and irregular by the adult standards. For a few days after birth, owing to the lessening in the metabolism from lack of assimilation, the degree of heat may fall a degree or so below the daily average of about 37.2° (99° F.). Exposure decreases the temperature readily. Raudnitz found that a cold bath raised the temperature (as indicated in the rectum) in vigorous newborn children, but lowered it in feeble infants. If we take 37.2° (99° F.) as the average temperature of the first ten years, it must be considered the same as all averages; that is, as more or less artificial. The causes of variation in temperature are numerous, and in childhood many of these frequently produce effects much more marked than among adults. Thus excitement, especially mental excitement, and intestinal irritation of a trivial degree, weak toxins, and fatigue, raise the temperature of the child of two or three years in a way not observed in the child of ten or in later life. This great variability is especially marked in girls; but in both girls and boys it constitutes the chief peculiarity of the temperature during childhood. A temperature of 39° (102.2° F.) in an adult usually means something of consequence, but in a three-year-old it often means nothing which a movement of the bowels will not promptly dispel. Here, as elsewhere, we see the signs of neural incompleteness and of nervous instability.

The *senses* of children are, in general, more acute than are those of adults, save in so far as training is involved in developing the actual sense-organs. Sensations, however, by themselves are of little use comparatively, aside from their meanings to the individual. The child is relatively deficient in this apperceptive power and does not know yet, moreover, how to use his senses to the best advantage. Thus the effective result of sensation in general in childhood is far below that of the adult, although the latter's actual sense-organs may be less perfect as mechanical instruments than are those of the child.

More marked, by far, than the bodily characters of childhood are those of the *mental aspects* of the individual when young. Into these, so amply discussed are they in pedagogical and psychological literature, we cannot go further here. Three principles, however, must be mentioned which are more or less important in medicine. First, the young child lacks mostly whatever degree of voluntary control over physiological and reparative process the adult mind exerts. This makes the child a more passive and more plastic patient as well as pupil. Its physiology is perhaps to be found in the incomplete command over the so-called "voluntary" musculature which is so conspicuous an aspect of childhood, already discussed above. How far this control extends over the vegetative functions in the clever and accomplished adult we do not as yet commonly appreciate.

Second, the child is relatively naïve and open to all kinds of influences. Habit in this period of life has not yet laid its all-encircling resistless fingers on the body and the mind. Children, therefore, are more amenable to all sorts of therapeutic and hygienic measures, and especially to those which like suggestion do their work through the mental processes.

Third, worry has not yet fixed its hold on the normally cared-for child. In the adult this is a source of harm whose importance it would be hard indeed to exaggerate. Chronic emotion of fear, as worry is, its asthenic effects on bodily processes are certain, and none the less so because the mode of its action is not fully made out. It is hard not to believe that worry through the trophic nerve-impulses depresses the metabolism and so undermines the resistance of many kinds of tissue. Working in the opposite direction of invigoration and stimulation, joy and happiness exert a wholly beneficial effect. Childhood, normally the joyful age in our too strenuous "civilized" life, receives the full benefit of this continual sthenic influence. Not a little of the versatile freshness of the child's bodily metabolism may come from this sort of mental stimulation—as it may come to all humanity centuries hence, when the old-time worries, largely based on the struggle for existence and good health, shall be outgrown. At present, as always, the great problem of hygiene and of therapeutics everywhere (though we scarcely realize it as yet) is how to *rejuvenate* in a useful way the mind and body of the experience-wise adult!

The mental development, so-called (really psychomotor evolution), of the average child has been carefully observed in a relatively few cases—and hundreds of such researches and accounts are necessary before we can begin really to understand the minds and the action-systems of children, as the bases of therapeutics (infantile and adult) and of education. There follows a chronological epitome of the evolution for the first three years of the girl "L." as discussed in the present writer's "Moto-sensory Development," (Baltimore, 1910). As a basis for comparison this epitone can hardly fail to be of value to physicians and to parents, as well as to teachers.

First Week.—Blinking, reflex, from stroking of nose. Coordination of eyes. Finger grasp, reflex. Inhibition, reflex, from touch sensations. Perceptions, reflex, of touch. Pursing, reflex, of mouth from touch on either lip. Shaking, reflex, of head. Sneezing. Suction, reflex, on fingers. Yawning. Hiccough. Reaction, sthenic, to light. Smile, reflex. Closing, reflex, of eyes to light. Inhibition, general reflex, from sound. Reaction to sound. Sounds perceived. Turning reflex, of head from light. Emotional facial reactions. Smile, spontaneous. Unpleasantness. Stretching, reflex, of body.

Second Week.—Drawing back, reflex, of head. Scratching, reflex, of own face. Vomiting, reflex. Extrusion, reflex, of nipple at satiety. Pleasantness reaction at a person's face. Raising, reflex, of arms, from noise. Touch reflex, fading of. Fright gasp. Groping, reflex, for breast. Eyes follow, reflexly, light. Frown. Internal strabismus. Perception. Sneezing, from light. Spreading, reflex, of toes, from touch. Unpleasantness of removal of fist from mouth. Eyes follow, reflexly, hand. Fixation of vision.

Third Week.—Replacing, reflex, of finger in mouth. Reaction to discomfort. Memory image. Laugh. Sitting attempts, reflex.

Fourth Week.—Reaching with arms, reflex. Recognition,(?) reflex, of bottle.

Seventh Week.—Pupillary reaction to light. Tears. Flexion, lateral and vibratory, of head, hanging free. Pleasantness of passive movement of limbs. Shaking of head, hanging free.

Eighth Week.—Abduction, reflex, of big toes from tickling of sole. Extension, reflex, of toes from tickling of sole. Flexion, reflex, of leg from tickling of sole. Holds head erect. Rhythmic reflex movements of four limbs from massage of abdomen. Squaring, emotional, of lower lip. Eyes follow, voluntarily. Heat, pleased enjoyment of. Seizing, impulsive, of left ear. (Habit fading.) Vocalization of ä. Opening eyes as sign of pleasure.

Ninth Week.—Breaking, passive, of habit complex. Taste. Anger in cry. Imitation, reflex, of gurgling. Recognition of mother. Smell, recognition of mother through(?)

Tenth Week.—Perception, conscious, of image in mirror. Grasping, reflex. Fear of passing people. Pain, crying from.

Eleventh Week.—Perception of tridimensional space (on 17th week). Reaching with arms, voluntary. Habit of posture. Rubbing knuckles in her eyes.

Twelfth Week.—Vocalization of ā, oo. Interest in own hand. Direction of sounds, perception of.

Thirteenth Week.—Fear of crackling of paper. Imitation, reflex, of shaking left hand.

Fourteenth Week.—Recognition of the unfamiliarity of a stranger.

Fifteenth Week.—Fear of piano music.

Sixteenth Week.—Sitting up, reflex, by drawing on arms.

Seventeenth Week.—Closing, voluntary, of lips against cold food (ice cream). Perception of coldness of food by lips. Recognition of own name. Accommodation, before this time, picking up, reflex, from touch stimulus. Sthenia, general, of redness.

Eighteenth Week.—Opening of hand, voluntary. Seizing, voluntary, of toes. Wink, reflex, from threatening movement.

Nineteenth Week.—Imagination. Inhibition, voluntary of wink-reflex. Rhythm, in babbling.

Twentieth Week.—Biting of fingers. Fear of water. Expectancy. Pulling, voluntary, of hair. Perception of similarity.

Twent-first Week.—"Brown study." Interest, voluntary. Comparison, deliberate, of an object and its mirror reflection. Conception of similarity. Wonderment. Attempt to stand.

Twenty-second Week.—Association of noise of hand-clapping and the movement. Repetition of actions. Conscious revery. Memory of antics. Rotation, voluntary, of hand. Smell.

Twenty-third Week.—Extension, voluntary, of trunk. Missing of water in bath-tub. Chewing, reflex, from hunger. Association of her name with herself. Sitting up, unassisted.

Twenty-fourth Week.—Delight at seeing mother again. Reaction time of voluntary grasp greater than that of reflex grasp.

Twenty-fifth Week.—Imitation, voluntary, with mouth. Shrugging of shoulders.

Twenty-sixth Week.—Discrimination of objects. Fear of dark. Fear of harsh noise. Support of her weight on feet. Walking, reflex. Fear of falling.

Twenty-seventh Week.—Creeping attempt. Discrimination of red from green. Perception of a hair.

Twenty-eighth Week.—Imitation, voluntary, of hand-waving. Attention, voluntary. Self-possession. Unpleasantness of the touching of fur, etc.

Twenty-ninth Week.—Desire grunt. Tearing, voluntary, of paper.

Thirtieth Week.—Vocalization, voluntary, variety in. Moral sense.

Thirty-first Week.—Inhibition, voluntary, to turn around. Discrimination of inflections. Dreaming. Grimaces. (Habit gone next week.) Sensibility to ridicule.

Thirty-second Week.—Fear of bunch of keys. Shaking, voluntary, of a rattle.

Thirty-third Week.—Discrimination of colors, red, yellow, and blue. Traction, voluntary, on string. Imitation, voluntary, of complex movements.

Thirty-fourth Week.—Swallowing, voluntary. Surprise. Conscious thought.

Thirty-fifth Week.—Marking, voluntary, with pencil. Association of an object and its name.

Thirty-sixth Week.—Traction, voluntary, on her own dress skirts to see feet. Vocalization of consonant.

Thirty-seventh Week.—Closing, clonic and voluntary, of right hand as sign of desire for an object.

Thirty-eighth Week.—"Destructiveness." Fear of shod foot.

Thirty-ninth Week.—Waving, voluntary, of hand for good-bye. Pity, from tone of voice.

Forty-first Week.—Use, spontaneous, of word papa.

Forty-third Week.—Imitation, voluntary, of guttural vocal. Dancing, reflex.

Forty-fourth Week.—Swinging of legs, voluntary. Waving, voluntary, of feet. Blowing, voluntary, through nose.

Forty-fifth Week.—Dancing, voluntary. Extension, voluntary, of tongue. Delight in association with another child.

Forty-sixth Week.—Vocalization, voluntary.

Forty-seventh Week.—Calling, voluntary, of a person.

Forty-ninth Week.—Play, imitative.

Fifty-second Week.—Ambidexterity. Blowing voluntary. Smell, disagreeable.

Fifty-third Week.—Jealousy. Understanding of pronouns.

Fifty-fourth Week.—Shaking, voluntary, of head with hands.

Fifty-fifth Week.—Creeping. Taste, disagreeable.

Fifty-eighth Week.—Delight in looking at pictures. Fear of the uncanny. Feeling of uncanniness. Conception of utility (of a pillow).

Fifty-ninth Week.—Bashfulness. Pouting. Suggestibility.

Sixtieth Week.—Anthropomorphism. Noise making, deliberate.

Sixty-first Week.—Standing, voluntary. Shaking, voluntary, of head.

Sixty-second Week.—Musical sense. Expression, voluntary, by facial expressions. Nodding in affirmation. Pretence.

Sixty-fifth Week.—Rolling, voluntary, of ball. Vanity. Vocalization of inflection.

Sixty-sixth Week.—Vocalization of liquid sounds.

Sixty-seventh Week.—Walking, voluntary. Laughter at picture of crying child.

Sixty-eighth Week.—Circular movements in drawing. Personal opposition.

Seventieth Week.—Use of "Doo!" in desire.

Seventy-first Week.—Talking in sleep. Eagerness for language. Effort unpleasant to imitate words.

Seventy-third Week.—Imagination, reproductive, of tune. Use, spontaneous, of "good night."

Seventy-fourth Week.—Conception of the meaningfulness of printed letters. Repetition of words.

Seventy-fifth Week.—Getting up, voluntary, to stand.

Seventy-seventh Week.—Conception of causality. Self-consciousness. Orderliness habit.

Seventy-eighth Week.—Discrimination of brightness (yellowishness).

Seventy-ninth Week.—Discrimination of colors other than red, yellow, and blue. Walking backward.

Eighty-first Week.—Catching of object let fall.

Eighty-second Week.—Closing, voluntary, of eyes.

Eighty-third Week.—Vocalization of sentence.

Eighty-fourth Week.—Wiggling, voluntary, of toes. Feeling and understanding of humor

Eighty-fifth Week.—Control, voluntary, of sphincters.

Eighty-sixth Week.—Conception of time. Use, spontaneous, of word tomorrow.

Ninety-first Week.—Perception, disagreeable, of wetness on fingers. Use of prepositions.

Ninety-eighth Week.—Disgust at mushy foods, etc.

One Hundred and Second Week.—Dreaming, recollection of.

One Hundred and Third Week.—Going upstairs. Perception, stereognostic. Absent-mindedness. Preference for redness.

One Hundred and Fourth Week.—Rotation movement with fingers. Understanding of the measurement of space. Use, spontaneous, of word yesterday.

One Hundred and Sixth Week.—Modesty, personal. Use of plural forms of words.

One Hundred and Tenth Week.—Conception of threeness. Use, spontaneous, of I.

One Hundred and Twelfth Week.—Conception of tomorrowness.

One Hundred and Eighteenth Week.—Comparison, deliberate, of faces, etc.

One Hundred and Twenty-first Week.—Counting to thirteen.

One Hundred and Fortieth Week.—Recognition of a melody.

One Hundred and Fifty-second Week.—Pretence of being someone else. Singing of a part of a tune rightly. Use of nonsense words.

There are two principles other than those noted above that are absolutely basal in the knowledge and science of childhood (in Europe often called Paidology) which the business of the average physician makes it essential that he should know more of than is usual; the widespread *secondary and tertiary sexual differences* in boys and girls from the very beginning on, and the equally comprehensive *contrast between childhood and adulthood* in many important respects. In elaborating these two principles and demonstrating them for the physician's practical use there is ample sanction for the writing of about the only kind of medical text-book not yet on the market, namely, a really adequate treatise wholly on the psychophysiology of the child. While child psychology is still in its earliest infancy, child physiology has not yet, strangely enough, even come to term. The reason is close at hand—few realize as yet how unlike the adult in nearly every way the child is; and how different are boys from girls in most important ways other than those primarily sexual.

Boas lays the anthropological basis, to a degree, of this latter matter in a little table and remarks giving the results of the observations available in this particular narrow field.

"It might seem," says Prof. Boas, "that the difference between the sexes does not develop until the period of adolescence; but a study of the eruption of the teeth which I made a number of years ago, and the more recent interesting investigations by Rotch and Pryor on the ossification of the carpus, show that the difference in physiological development between the two sexes begins at a very early time, and that in the fifth year it has already reached a value of more than a year and a half.

"I give here a tabular statement of the available observations:

	Age in years.		Difference.
	Boys.	Girls.	
Ossification of scaphoid	5.8	4.2	−1.6
Ossification of trapezoid	6.2	4.2	−2.0
Eruption of inner permanent incisors	7.5	7.0	−0.5
Eruption of outer permanent incisors	9.5	8.9	−0.6
Eruption of bicuspids	9.8	9.0	−0.9
Minimum increase of annual growth	10.3	8.2	−2.1
Eruption of canines	11.2	11.3	+0.1
Maximum increase of annual growth	13.2	11.2	−2.0
Eruption of second molars	13.2	12.8	−0.4
Maximum variability of stature	14.8	12.4	−2.4

These data are not very accurate and must be considered a first approximation only."

Every bisexual table of growth in stature and weight, every physiological research in which both sexes serve as subjects, etc., etc., only enlarges this early and late basal difference. In the psychological realm the conditions are exactly the same, certainly not less conspicuous. Medically and pedagogically appreciation of this general fact is long overdue; when it arrives in the common knowledge, many minds will rapidly supply the details, and soon practical medicine and hygiene, as well as education, will have taken one more stride forward, toward universal normality.

Knowledge of the contrast between the child and the adult seems to be passing through the same evolution as the realization of the thorough-going difference in the sexes. The text-books of pediatrics must be compared at present with those on adult practice and therapeutics, etc., if one would learn the differences in drug susceptibility, and so forth, between child and adult. But the direction in which the average medical man most needs a hint apropos of childhood, perhaps, is the extreme liability of even the normal child to fatigue of a mental kind. Here the average physician is certainly an unwitting accomplice of the average school-teacher. Muscular fatigue takes care of itself by disposing to abundant sound sleep and thus often is almost a benefit, but mental fatigue has little or none of this action and is "all to the bad." Every measurement of school fatigue (*e.g.* by Claparède and by Binet) shows how real it is and psychophysiology demonstrates its harmfulness. It is the privilege of the American medical men and women to urge the reform of our public-school system so that it shall conform, somewhat at least, to our advancing knowledge of the real (as opposed to the traditional) child. *Children are not little men and little women*, but *children*, each peculiar to himself—and the most important and the most valuable things in the world. To realize in a scientific manner and degree their juvenile characteristics is the first necessary step toward the attention and the study which their preeminent importance in this world demands.

George V. N. Dearborn.

Chilodon.—A genus of ciliated protozoans which are oval, broad, flattened on the ventral surface, have the dorsum strongly arched, and the cytopharynx much curved. They are usually free living but have been found as accidental parasites in the human intestine in a case of dysentery. See *Protozoa*. A. S. P.

Chimaphila.—*Pipsissewa; Bitter* or *False Wintergreen; Prince's Pine.* The dried leaves of *Chimaphila umbellata* (L.) Nutt. (*Pyrola umbellata* L.; *C. corymbosa* Pursh.—fam. *Pyrolaceæ*).

This very pretty little plant, native of dry woods throughout the cooler regions of almost the entire North Temperate zone, is an herb-like undershrub, having an erect stem a few inches in height, arising from a short, prostrate portion. The leaves are crowded near the ground and the scape bears several very pretty, five-merous, wax-like, white, subpendulous flowers, about a half an inch broad. The leaves are from 2.5 to 5 centimeters (1 to 2 in.) long and 1 to 1.5 centimeter (⅜ to ⅝ in.) broad, oblanceolate, the lower half cuneate and entire, the upper coarsely and sharply serrate, acute or obtusish, thick and rigid, brittle, above dark-green or brownish-green, and slightly shining, the veins strongly impressed, underneath paler, the veins very prominent; odor very slight, tea-like; taste astringent and bitterish.

The constituents are almost identical (as are the properties and uses) with those of *Uva Ursi*. There is between four and five per cent. of tannin, arbutin, sugar, gum, etc., and a small amount of the yellow, crystalline, neutral substance, *Chimaphilin*, which is inodorous and tasteless, soluble in alcohol, ether, and chloroform, but only slightly soluble in water. For its mildly astringent and diuretic properties and uses, see *Uva Ursi*. The Pharmacopœia provides a fluid extract, the dose of which is fl. ʒ ss. to i. (2.0–4.0).

Henry H. Rusby.

Chinaphthol.—Betanaphthol alpha-monosulphonate of quinine, $(C_{10}H_6OHSO_3H)_2$. $C_{20}H_{24}N_2O_2$. This is a yellow crystalline powder of bitter taste, insoluble in cold water, somewhat soluble in hot water and alcohol, and containing about forty-two per cent. of quinine. Riegler states that in the intestines it is decomposed into quinine and naphthol-sulphonic acid, and therefore is both an intestinal antiseptic and an antipyretic. He has used it with satisfaction in typhoid

fever, dysentery, intestinal tuberculosis, and acute rheumatism, in daily dosage of gr. viij. to lxxv. (0.5–5.0). W. A. Bastedo.

Chinaseptol.—($C_9H_5.OH,SO_3HN$.). Diaphtol, ortho-oxychinolin-meta-sulphonic acid. This occurs in yellowish crystals melting at 295° C. (563° F.), and is slightly soluble in water, the solution turning green with ferric chloride. Chemically it bears the same relation to chinolin as phenol-sulphonic acid bears to benzol. It is used as a non-poisonous antiseptic or as a substitute for salol. W. A. Bastedo.

Chinoidine.—See *Cinchona.*

Chinoline.—See *Quinoline.*

Chinosol.—The neutral oxychinolin sulphate, $(C_9H_7ON)_2H_2SO_4$, and the potassium salt are both known as chinosol. Both are yellow crystalline powders of feebly aromatic odor, freely soluble in water and insoluble in alcohol and ether. Their dilute aqueous solution turns green with ferric chloride, and forms a green coating on steel instruments. Chinosol is stated to be a more powerful antiseptic than bichloride of mercury, with great penetrating power, and is highly spoken of by European clinicians; a 1–500 solution killed the plague bacillus in ten minutes. It has been used with advantage by Gilles in vaginitis in strength of 1 to 8,000 to 1 to 1,000, also in leprosy and bone tuberculosis. Mixed with five to ten per cent. of boric acid it may be used as an antiseptic powder in place of iodoform. Hobday found it a powerful disinfectant for the hands, the site of operation, and sutures, a solution of 1 to 60 producing no irritation. For cellulitis or other severe infection it should be used in strength of 1 to 500, but for ordinary use 1 to 1,000 is better. Cipriani recommends it by mouth and hypodermically for tuberculosis. It has lso been used as an antipyretic. Hobday's experiments on cats indicate the limit of safe dosage to be gr. $\frac{1}{15}$ (0.0037) per pound (400.0) of body weight. Cadavers are said to be effectively preserved by intraarterial injection of five-per-cent. solution.

Pulvis chinosol composita consists of chinosol, chinaseptol, talc, and silica. W. A. Bastedo.

Chirata.—*Chiretta.* The entire plant, *Swertia chirayita* (Roxb.) Hamilton (fam. *Gentianaceæ*).

Chirata is a native of Northern India, especially in mountainous districts in Nepal, where it is found at an elevation of from five to nine thousand feet. Its use was introduced from India, where it has been long employed, into European medicine about fifty years ago.

The plant is gathered when fully grown; the flowering stems being pulled up entire, dried, and tied into long bundles.

Root nearly simple, about seven centimeters long; stem branched, nearly one meter long, slightly quadrangular above; containing a narrow wood circle and a large yellowish pith. Special attention should be given to this large pith, as there is a spurious article which is destitute of it, being quite hollow. Leaves opposite, sessile, ovate, entire, five-nerved. Flowers numerous, small, with a four-lobed calyx and corolla. The whole plant smooth, pale brown, inodorous, and intensely bitter.

In composition, Chirata is almost the exact equivalent of gentian, as it is also in properties and uses. Bitter *ophelic acid* ($C_{13}H_{20}O_{10}$), soluble in both alcohol and water, replaces the gentisic acid of the latter, *chiratin* ($C_{26}H_{48}O_{15}$), a yellow, bitter, crystalline glucoside, soluble in warm water and alcohol, replaces gentiopicrin, and as with gentian, there is no tannin, though ferric salts produce a dark color, without inky precipitate.

Chirata is a simple bitter and tonic. We have official a fluid extract, dose fl. ʒ ½ to i. (1.0–4.0), and a ten-per-cent. tincture, made with sixty-five-per-cent. alcohol, dose fl. ʒ ¼ to ij. (1.0–8.0). The latter is much the better preparation, especially in small doses. Henry H. Rusby.

Chitin forms the chief organic basis of the shell of cephalopods, etc., and it probably exists in combination with a protein-like substance. Chitin is characterized by being very insoluble, although on boiling with mineral acids it yields a compound, chitosan, which on further decomposition gives rise to glucosamine. Frank P. Underhill.

Chitosamine.—See *Glucosamine.*

Chlamydobacteriaceæ.—A family of the higher bacteria, in Migula's classification, occurring just below the Hyphomycetes. They are cells of various shapes, forming branched or unbranched chains, enclosed in capsules or sheaths. The following genera are included by Migula in this family. Cladothrix, Crenothrix, Phragmidiothrix, Streptothrix, and Thiothrix. The grouping is, however, rather uncertain, and several of these genera are classed by Zopf under Leptotricheæ; a number are placed definitely among the Hyphomycetes or moulds. T. L. S.

Chlamydophrys.—A genus of rhizopods in which the animals are provided with a transparent silicious shell. These protozoans have been found in the feces of many vertebrates including cow, guinea-pig, turtle, and man. See *Protozoa.* A. S. P.

Chloasma.—*Synonyms:* Liver Spot, Moth Patch, Mask; Fr., *Chloasme;* Ger., *Pigmentflecken.*

Definition.—An abnormal pigmentation of the skin occurring usually in patches of yellow, brown, or black color, of various shapes and sizes.

It is used as a generic term and includes all discolorations of the skin, either circumscribed or diffuse, which are not accompanied by any other apparent objective changes. The color is of a yellow, brown, or black, changing in some conditions to a bronze or black (melanoderma). The discolorations may be unilateral, irregular, or symmetrical in their distribution, consisting of patches or of more or less diffuse pigmentations, stopping abruptly at the border, or they may shade off into the normal color of the part

Varieties.—Chloasma is usually divided into the idiopathic and the symptomatic varieties.

Idiopathic chloasma is due to external causes or irritants: (1) Mechanical; (2) chemical; (3) thermal; (4) parasitic.

1. *Mechanical.*—As a result of abrasions and of trauma, and also in consequence of scratching, in pruritus senilis, prurigo, and other pruriginous diseases, deep pigmentation occurs in certain individuals, especially the run-down and elderly.

2. *Chemical.*—In this class may be placed those cases in which pigmentation follows sinapisms, vesicants, and counterirritants. It is a question whether this is due directly to chemical effect or merely to the irritation. Tattooing may be placed here.

3. *Thermal.*—Bronzing following the erythematous stage of sunburn is not a true chloasma; it is simply a pigmentation of the exposed parts—deep brown in the case of blondes—produced by the sun's rays, and occurring generally in rather large and well-defined areas. Older people of a certain type have a tendency toward patchy pigmentation of the neck, arms, hands, and face, which is undoubtedly excited and increased by the sun's rays. Stokers and those exposed to hot fires often have peculiar darkened areas upon the ex-

posed parts. Cold has been known to produce like conditions.

4. *Parasitic.*—De Amicis has lately described a peculiar café-au-lait pigmentation upon the chin and lip, due to the demodex folliculorum. Majocchi has likewise seen two cases. Pityriasis nigricans (Willan) is the deep pigmentation seen in vagrants and tramps, produced by scratching and generally due to pediculi corporis.

The various fungi which flourish upon the skin and cause yellowish or brownish spots, such as tinea versicolor, erythrasma, mal del pinto, are described under their respective titles.

Symptomatic chloasma may be a sequel of, or accompany, certain physiological or pathological conditions of the system.

After certain inflammatory skin diseases—*e.g.* dermatitis herpetiformis, psoriasis, lichen planus, eczema, syphilitic eruptions, etc.—the sites occupied by the former eruption often display a yellow or brown pigmentation, a part of which is of hematogenous origin, while another part comes from the cells of the locality.

In cases of varicose veins the legs often have a deep patchy brown color, beginning about the follicles.

Chloasma uterinum is either a physiological or a pathological condition. Pregnant women usually have a deepening of the color, in pigmented portions of the body, of a greater or lesser degree. They also sometimes are affected with an abnormal deposit of pigment, which occurs in patches of a dirty yellow to brown color over the face, especially on the forehead, cheeks, and chin. Often it becomes diffuse in the shape of a sharply defined mask, the so-called *masque des femmes enceintes.*

In uterine and ovarian diseases a similar condition may be seen, the pigmentation occurring either in spots or in the form of a diffuse mask. In the latter case the neck is especially involved, though in this location the rough and tightly fitting ruffle or neck ornament may be a contributing factor.

In all cases of pigmentation of the face and neck the uterus and ovaries should be examined.

Various blood diseases of unknown origin (hematochromatoses of von Recklinghausen) are sometimes accompanied by abnormal pigmentation of the skin.

In exophthalmic goiter, abnormal pigmentation, in the form of patchy or diffuse freckles, is quite common, especially along the course of the musculocutaneous nerves on the hands and arms, and over those parts of the face which are supplied by the fifth nerve (Blake).

In abdominal tumors, tuberculosis, cancer, and lymphoma, pigment is common on the face and hands.

Diseases of the liver give rise more often to jaundice, but they are also accompanied by a patchy or diffuse pigmentation of the skin, often simulating, in this respect, Addison's disease, as is seen in diabetic cirrhosis.

It was formerly the fashion to ascribe, in a general way, all "moth spots" or patchy pigmentations to liver disorders (so-called "liver spots"). This idea was erroneous, for the pigment due to liver diseases is deposited more or less generally, and not in sharply circumscribed spots or patches, as is the case in the so-called "liver spots." These remarks may also be applied to malarial pigmentations, which are produced by chronic malarial poisoning.

Diseases of certain glands—*e.g.* the suprarenal (Addison's disease) and the thyroid (Graves' disease) glands—are accompanied by dyschromias.

Pigmentations of varying degree and extent have been observed in cases of melanotic cancer and also in those of other forms of malignant growths.

Cachectic conditions often produce a universal deepening of pigment, from a sallow yellow to a yellowish-brown color. This is particularly true of tuberculosis, chronic rheumatism, syphilis, and leprosy; in the last-named disease the pigmentation is quite marked about the face and extremities in the late stages.

It is a fact which is often overlooked that gastrointestinal disorders play a rôle in certain cases of chloasma. Chronic constipation and intestinal and gastric fermentation of a chronic character in which certain poisonous bodies are absorbed, produce besides other symptoms a patchy pigmentation of the face and hands, which is almost always symmetrically distributed.

Syphilitic pigmentation of the neck, usually seen in women, is accompanied by other local symptoms and does not belong here.

In respect to drugs, the most important discoloration is produced by nitrate of silver, for which see *Argyria.*

Arsenic also produces a brown or bronze pigmentation of the face, neck, and abdomen after prolonged administration of the drug, but, as I have endeavored to show, this is not an essential primary pigmentation, for it is always preceded by a sensible degree of inflammation of the skin.

Pathology.—Little is known of the histopathology of chloasma. The pigment, in the more superficial forms, is deposited in the epidermis, either as something which was not there before, or else as an addition to a previously existing deposit; but in many varieties the cutis also contains a great amount of yellow granules, either in connective-tissue cells, which may form pigment themselves, or in the lymph spaces.

Van der Vegt found that in sections the epidermic pigment was soluble in a weak solution of caustic potash in peroxide of hydrogen, while that of the cutis was not soluble in this solution, though perfectly so in strong hydrochloric acid.

Treatment.—The treatment of chloasma consists simply in properly treating the cause or the disease upon which it is dependent. Consequently the reader is referred to the different articles which treat of the various conditions above mentioned. But no matter what the cause may be, the pigment is always slow to disappear; however, local treatment may in some cases assist in its removal. The results from local treatment depend, of course, upon the depth and location of the pigment. The remedies commonly used for this purpose cause desquamation of the epidermis, thus attempting by the desquamation to remove the pigmented cells. Some of these remedies are also supposed to have a bleaching effect, which at least is doubtful.

If after a thorough trial of the usual remedies no marked improvement is perceptible, treatment should be discontinued, as this probably shows that there is a deposit in the cutis, and such a deposit is often increased by continued irritation. Even in cases in which the spots are removed, there is often a reappearance with increased pigmentation.

The smaller areas can be very effectually removed by electrolysis, by inserting the needle just to the cutis margin, or by quick successive superficial stabs of the instrument.

Peroxide of hydrogen is recommended. It should be applied on cotton and allowed to remain on the spot several minutes. This procedure may be repeated several times a day. Applications, cautiously made, of the carbon dioxide snow sometimes seem to be useful. Trichloracetic acid barely brushed over the surface and not allowed to run over the contiguous skin, and carbolic acid similarly employed, are useful in limited patches.

The various scaling agents used are: salicylic acid in a saturated alcohol solution or in a paste; resorcin in from ten- to twenty-per-cent. solution in alcohol or in a paste; corrosive sublimate, one per cent. in almond emulsion; and nightly frictions of green soap. The following prescription is to be recommended:

℞ Hydrargyri ammoniati
Bismuthi subnitratis . . ää gr. xl.
Vaselini . . . . . ʒ i
Olei rosæ . . . . q. s.
M. Sig.: Apply gently to the discolorations at night, and wash off in the morning with green soap.

This ointment in the course of time will materially lighten the patches, and is greatly to be preferred to the strong lotions of corrosive sublimate, which often produce disastrous results.

William A. Hardaway.

Chloral.—By the term chloral is ordinarily meant not what is, chemically speaking, chloral proper, but an entirely distinct body, chloral hydrate or hydrated chloral, the *Chloralum Hydratum* of the U. S. P. Chloral proper, C_2HCl_3O, is, chemically, acetic aldehyde (common aldehyde) with three atoms of hydrogen in the molecule replaced by chlorine. Its chemical name is, therefore, trichloraldehyde, and its constitutional formula $COH.CCl_3$. It is a thin, oily, colorless, heavy fluid. On mixing chloral with water the two bodies unite, forming a crystalline hydrate of chloral, C_2HCl_3O, H_2O, which is the substance used in medicine under the misnomer *chloral*. Chloral hydrate, or "chloral," appears in "separate, rhomboidal, colorless, and transparent crystals, having an aromatic, penetrating, and slightly acrid odor, and a bitterish, caustic taste; slowly volatilized when exposed to the air. Freely soluble in water, alcohol, or ether; also in chloroform, benzene, petroleum, benzin, carbon disulphide, fixed and volatile oils. It liquefies when triturated with about an equal quantity of camphor, menthol, thymol, or phenol. When dried and heated to about 58° C. (136.4° F.) it melts, forming a liquid having a specific gravity of about 1.575, which at a higher temperature should not evolve inflammable vapors. Liquefied hydrated chloral solidifies to a crystalline mass between 35° and 50° C. (95° and 122° F.). Hydrated chloral is decomposed by caustic alkalies, alkaline earths, and ammonia, chloroform being formed, and a formate of the base produced. A freshly prepared aqueous solution of hydrated chloral is neutral, but gradually acquires an acid reaction." (U. S. P.) Chloral hydrate should be kept in glass-stoppered bottles in a cool and dark place.

The effects of chloral hydrate upon the animal economy, while much resembling those of chloroform, yet differ therefrom in many marked respects. Chloral hydrate, like chloroform, is locally a sharp irritant, and constitutionally a powerful neurotic, capable of producing arrest of the more important of the nervous functions, and so death. The most important difference between the action of chloral and that of chloroform is that the former drug has, relatively, a greater tendency to determine sleep, depression of respiration, and fall of temperature, and a distinctly less pronounced power to dull sensation, than has chloroform. The pharmacopœial dosage is gr. xv. (1.0), and ordinarily the dose for an adult should not exceed gr. xxx. (2.0). Often twice and three times that quantity is well tolerated, but until the individual susceptibility of a given subject is tested, it is best to prescribe the smaller doses. The remedy is given in solution, with the sharp twang of the taste disguised by some syrupy and aromatic addition. In ordinary medicinal dosage of gr. xv–xxx. (1.0–2.0), the only marked effect of chloral hydrate is a gentle, calm, agreeable, dreamless sleep, which, if induced at bedtime, will, unless there be special reasons to the contrary, probably last till morning, and from which the waking will be natural, unattended by the disagreeable by-effects of an opiate. During the chloral sleep, forced awakening is as easy as during a natural heavy sleep, and the subject, when roused, is perfectly rational. Pulse and respiration are a little slowed, but otherwise the functions are not obviously affected. In increased dosage natural sleep deepens into coma; respiration, blood pressure, and pulse rate are markedly depressed, or the heart's action may be rapid while weak; temperature distinctly falls; sensation, after an initial temporary hyperesthesia, becomes moderately blunted; motor paralysis, voluntary and reflex, comes on, and, if the dose has been sufficiently large, death ensues by failure of respiration; or, if the action has been sudden and overwhelming, death is by syncope as in shock. The principal postmortem revelation in fatal chloral poisoning is congestion of the lungs and of the cerebrospinal axis. These various phenomena are undoubtedly produced by a direct action of the poison upon the nerve centers presiding over the functions deranged. Of the effects, those of greatest clinical importance are the hypnotism and the paresis of the respiratory center and of the motor tract of the spinal cord generally.

When chloral hydrate is taken habitually, certain peculiar effects may follow. Perhaps the most common is some form of skin eruption, which is generally erythematous, though sometimes papular. In certain subjects, urticaria or purpura may result; in other cases, conjunctival or faucial irritation; in still others, dyspnea; and in unique cases, pa ns in all the limbs and partial paraplegia have clearly been traced to chloral poisoning (Anstie). Quite a common effect, seen even in cases of single dosage, is one where chloral and alcohol have been taken together, namely, deep flushing of the face and throbbing of the vessels, exactly as produced by amyl nitrite. Prolonged habitual use of the drug probably tends to debase the mind and morals of the subject in the same manner as indulgence in alcohol, ether, or chloroform; and sudden discontinuance, after a fixed habit of excess, may naturally lead to the same consequences as the sudden breaking of a pronounced alcohol habit.

In the matter of toxicology, cases of fatal or of even dangerous poisoning have generally resulted from inadvertent medicinal overdosage. The smallest authenticated fatal dose is twenty grains (1.3 grams), and the fact that such dose—one less than the usual medicinal dose—has killed only emphasizes the fact, now pretty generally recognized by the profession, that individuals show very different degrees of susceptibility to the action of chloral hydrate. The condition of dangerous poisoning is one of narcosis, distinguishable from the narcosis of opium, with which it is most likely to be confounded, by the conditions of the pupils. The pupils, in chloral poisoning, are either dilated, or if contracted are but moderately so, and dilate upon the subject's awakening. Very often, also, in chloral narcosis, the face is deeply flushed and somewhat bloated, the lips and eyelids swollen, and the eyes blood-shot. The treatment of poisoning by chloral hydrate is to evacuate the stomach, best by the stomach tube, and to sustain the flagging lungs and heart by artificial respiration. Medicinal respiratory and cardiac stimulants, though theoretically indicated, are practically of little use, because of the already hopelessly paralyzed condition of the tissue upon which they are to act.

Therapeutically, chloral hydrate is available to procure sleep, to oppose spasm, and to blunt pain. As an hypnotic it takes front rank among medicines, because of the combined certainty and yet pleasantness of its action. Yet the indiscriminate use of the drug in all conditions of wakefulness may easily work great harm. Thus, remembering the strong specific action of chloral hydrate to depress respiratory activity, it is plain that in the restlessness and wakefulness that result from dyspnea, in such conditions as congestion of the lungs, emphysema, or bronchitis with obstructed circulation, the drug is the most improper thing that could be prescribed.

Similarly, from its associated cardiac depression, all conditions caused or attended by feeble or embarrassed circulation contraindicate chloral. As an antispasmodic, chloral hydrate is peculiarly appropriate when the cause of the spasms is morbidly excited reflex irritability of the nerve centers. In tetanus it has thus worked many cures. As an anodyne this remedy is inferior to many others, as might be inferred from the fact, already mentioned, that anesthesia is not a very pronounced element of its physiological operation.

A special use of chloral hydrate, not medicinal, yet utilized by the physician, is as a preservative. Like the related substances, the volatile alcohols and ethers, chloral hydrate is markedly antiseptic, and possesses the peculiar feature that, while preserving putrefiable tissues from decay, it yet does not obviously change the physical appearance of even the most delicate structures. The agent is, therefore, peculiarly useful as a preservative for urines set aside for microscopical examination. As much of the drug in crystals as will lie on the thumb-nail added to about 100 c.c. (about fl. ℥ iij.) of urine will preserve the same perfectly for days or even weeks, and that, too, without affecting the ready recognizability of casts, blood or pus corpuscles, epithelial scales, or spermatozoa. The addition does not affect the heat and nitric acid test for albumin, but it vitiates the test for sugar by Fehling's solution, since a solution of chloral hydrate of sufficient concentration will itself reduce the copper of that test fluid. The antiseptic action of chloral hydrate is available for use in surgery, and lotions of from one to three per cent. strength have been proposed for wounds. Such weak percentages are necessary, else the application will smart and perchance develop constitutional poisoning by absorption. EDWARD CURTIS.
R. J. E. SCOTT.

Chloral Alcoholate.—This body, $C_2HCl_3O.\ C_2H_6O$, forms during the process of manufacture of chloral from alcohol. It is in white crystals, distinguished from those of chloral hydrate by their insolubility in cold water, although they melt on admixture with hot water. This body is not used as a medicine. Its chief interest arises from the fact that it is formed on adding chloral hydrate to alcoholic liquids, and that it causes rapid coma and collapse. Chloral hydrate added to beer or whiskey makes the well-known "knock-out drops" which are used for criminal purposes. W. A. BASTEDO.

Chloralamid.—See *Chloralformamidum.*

Chloral-Ammonium is obtained by passing dry ammonia gas through a solution of chloral in chloroform. It forms colorless needles melting at 84° C. (183.2° F.) and is almost insoluble in water. Boiled with water it forms chloroform and ammonium formate. It is given as an analgesic and hypnotic in dose of gr. xv.–xxx. (1.0–2.0).
W. A. BASTEDO.

Chloral Camphor.—This name has been applied to the clear fluid that results from trituration of equal parts of chloral hydrate and camphor. In the National Formulary of 1906, it bears the name of camphorated chloral. It is soluble in alcohol, ether, glycerin, and fixed oils, but on mixture with water suffers precipitation of the camphor. It possesses the medicinal properties of its ingredients, and in a teaspoonful dose in one case produced severe, irritant, and narcotic poisoning. Practically its only use is externally as a counterirritant in toothache and various muscular and neuralgic pains. W. A. BASTEDO.

Chloralformamidum.—Chloralformamide or, as it was formerly called, *chloralamide*, is "a crystalline solid made by the direct union of formamide and anhydrous choral." (U. S. P.) Its formula is $CCl_3CH_2OH.CONH_2$. The production of this compound is due to the efforts of chemists to introduce into choral some known stimulant to overcome the depression of the circulation that accompanies the use of choral. In addition to this absence of a depressing effect, other advantages over choral are claimed: It is much less disagreeable in taste and more soluble, characteristics which render it easy of administration. It is less irritating to the stomach, does not derange the digestive organs, and seldom causes headache, giddiness, or any disturbance of the nervous system.

It occurs in white crystals which have a faintly bitter taste and no odor, and are neutral in reaction. It is soluble in ten parts of cold water and in one and a half parts of alcohol. The salt should never be dissolved in hot water, nor heated above 120° F., as at that temperature it is decomposed. It is also decomposed by alkalies and alkaline carbonates. It is compatible with weak acids, which increase its solubility and render the solution more stable.

Chloralformamide is employed as a sedative and hypnotic in all the conditions in which chloral hydrate is indicated; notwithstanding its reputed safety when there is cardiac weakness, it is advisable to employ it in such cases with caution.

The dose advised by the pharmacopœia is gr. xv. (1.0), and this should be used to start with. The dose usually employed is somewhat larger, being about gr. xxx. (2.0). As a rule, it is advisable to begin with a smaller dose of gr. xv. to gr. xx. (1.0–1.3), when the insomnia is not accompanied by pain or excitement. On account of its solubility in alcohol, chloralformamide is easily given in solution diluted with some aromatic elixir. It may also be given in cachets. For whooping-cough and other spasmodic affections, it is given in doses of gr. ij. (0.12) every two hours. R. J. E. SCOTT.

Chloralose.—$C_8H_{11}Cl_3O_6$, anhydro-gluco-chloral. By heating chloral and glucose together for an hour at about 96° C., chloralose and parachloralose are formed. The latter is not use in medicine. Chloralose occurs in fine, colorless needles or small crystals of bitter, unpleasant taste, soluble in 170 patrs of cold water and readily soluble in hot water or alcohol. The crystals melt at 184°–186° C. (363.2°–366.8° F.). Following experiments on dogs, it was introduced in 1893 by Hanriot and Richet as a certain hypnotic devoid of depressing effects on respiration and circulation. In 1897 following experiments on man, Richet again recommended it highly, yet subsequent investigations have shown it to be extremely variable in its effects, and even unsafe in so small a dose as eight or ten grains. It is said to cause nausea, vomiting, slow weak heart, involuntary urination during sleep, and various nervous symptoms, such as delirium, tremors, and paralysis. The dose is gr. iij.–viij. (0.2–0.5).

By treating arabinose and xylose in the same manner as glucose, the above investigators have obtained analogous compounds named respectively arabinochloralose and xylochloralose. The former is stated to produce quiet sleep without nervous symptoms and to be much less toxic than chloralose. Xylochloralose, however, was found to be more toxic and less hypnotic. W. A. BASTEDO.

Chloraloximes are compounds of chloral with various oximes. They are nearly insoluble in water, decomposed by hot water, and soluble in alcohol. The principal ones are chloralacetoxime, chloral-camphoroxime, chloral acetaldoxime, chloral nitroso-

betanaphtholoxime, chloral benzaldoxime, and chloral acetophenonoxime. They all act as hypnotics.

W. A. Bastedo.

Chloralum Hydratum (U. S. P.).—See *Chloral.*

Chlorates are the salts of chloric acid, $HClO_3$. Only the potassium and sodium chlorates are used in medicine.

Potassium Chlorate: $KClO_3$. The salt is official in the United States Pharmacopœia under the title *Potassii Chloras*, Potassium Chlorate. This is a permanent salt, occurring in colorless, shining, prismatic crystals or plates, odorless, and having a cooling, saline taste. It dissolves in 16 parts of cold water, but in 1.7 parts of boiling water; insoluble in absolute alcohol, and but slightly soluble in diluted alcohol. If heated or triturated with organic substances, such as sugar, tannic acid, or cork, or with easily oxidizable chemicals, such as sulphur or phosphorus, a dangerous explosion is likely to occur. The salt should, therefore, be kept in glass-stoppered bottles and handled with care.

The chemical relationship between chlorates and nitrates is paralleled, as usual in such cases, by resemblance in physiological action. (See *Potassium.*) The present salt thus closely resembles niter in its effects, the principal difference being in intensity of power, the chlorate being the weaker—a fact probably in part due to the less ready solubility of the salt. Yet the chlorate is strong enough, in full concentrated dose, to be fatally poisonous, with symptoms of intense gastrointestinal irritation, and, in too lavish medicinal use, as was once the fashion in diphtheria, to be the likely cause of much of the nephritic disorder thoughtlessly attributed to the disease instead of to the medicine. For, like the nitrate, the chlorate of potassium has a distinct tendency to irritate the kidneys. Potassium chlorate does not give up its oxygen in the system, as was formerly believed. The only rational place of this salt in medicine hinges on the following fact: The chlorate is largely eliminated by the salivary glands, and probably also by the mucous follicles of the mouth and pharynx, and in inflammatory conditions of the surface textures of these parts distinctly tends to healing. Sore mouth or sore throat, catarrhal or ulcerative, is therefore treated with advantage with potassium chlorate in the form of wash or gargle, or in tablets with or without the addition of borax; these tablets should be allowed to dissolve in the mouth, and are not to be swallowed whole. A convenient practice is to prescribe a five-per-cent. aqueous solution of the salt, which is upon the verge of a saturated solution, and direct this to be used as a mouth wash or gargle every two hours, and at the same time a couple of teaspoonfuls to be taken internally. Such quantity will represent about 0.50 gram (gr. viij.) of the salt—a moderate single internal dose. Of preparations, the United States Pharmacopœia makes official *Trochisci Potassii Chloratis*, Troches of Potassium Chlorate, the ingredients being the salt, sugar, and tragacanth. Each troche contains 0.15 gram (about gr. ijss.) of chlorate. In ordinary sore throats or sore mouths, for the treatment of which affections the preparation is especially intended, these lozenges, if allowed to dissolve naturally without chewing, may be taken occasionally through the day.

Sodium Chlorate: $NaClO_3$.—The salt is official in the United States Pharmacopœia as *Sodii Chloras*, Sodium Chlorate. It occurs in colorless, transparent tetrahedrons of the regular system, permanent in dry air. It is odorless, with a cooling saline taste. It dissolves in about 1 part of cold water, and readily in boiling water. It is sparingly soluble only in cold alcohol, and dissolves in about 40 parts of boiling alcohol; it is also soluble in about 5 parts of glycerin. If mixed with organic substances or with readily oxidizable chemicals, such as sulphur or phosphorus, trituration or concussion may cause a dangerous explosion, as in the case of potassium chlorate. Sodium chlorate should be kept in glass-stoppered bottles. Sodium chlorate has the peculiar medicinal properties of the potassium salt except in regard to the effect of potassium compounds as such. It is important only because of its excess of solubility as compared with potassium chlorate. The medicinal uses are the same as those of the latter-named salt, which see above.

Toxicology.—Owing to its frequent use in medicine potassium chlorate is responsible for quite a number of poisonings. The sodium salt can be ignored in this connection. The *symptoms* are those of gastrointestinal irritation, severe abdominal pain, vomiting, and diarrhea. The effect on the blood is peculiar; it exerts a hemolytic action in the red blood corpuscles, and converts the hemoglobin into methemoglobin. Other changes chiefly of a degenerative kind have been noted in the blood. At autopsy, the blood is of a chocolate-brown color. The poison is eliminated almost entirely by the urine, and very slightly by the saliva. The minimum lethal dose is given by Witthaus as approximately three drams (twelve grams) for an adult, one and a half drams (five grams) for a child, and fifteen grains (one gram) for an infant. But over 700 grains have been taken without causing death. The same authority outlines the *treatment* as follows: "Emetics should be given or the stomach washed out. Excretion by the saliva may be stimulated by hypodermics of pilocarpin. Stimulants and digitalis are indicated. Inhalation of oxygen may be serviceable. Transfusion of blood was tried in one case with results beneficial at first, but afterward not so favorable, and without saving the patient." The chief pathological changes are found in the blood, kidneys, and spleen.

R. J. E. Scott.

Chloretone.—Aneson, anesin, acetone-chloroform; tertiary trichlorbutylalcohol, $(CH_3)_2C.OH.CCl_3$. Potassium hydroxide is slowly added to a mixture of equal weights of acetone and chloroform, and then steam is blown through. The resulting chloretone forms a white crystalline mass resembling camphor and having a camphoraceous odor. It is slightly soluble (1 in 200) in cold, more so in boiling water, is fairly soluble (1 in 10) in glycerin, and freely soluble, (3 in 2) in ninety per cent. alcohol, and in ether and chloroform. It is decomposed by strong sulphuric acid, but is not affected by weak acids or alkalies.

Chloretone is antiseptic, locally anesthetic, and hypnotic. Combining the properties of an antiseptic and an anesthetic, it is of considerable value in minor surgery. Kossa and Vamossy found it to be slower in its action than cocaine, and somewhat less penetrating; yet it had more anesthetic power, as a one-per-cent. solution was equivalent to a 2.8-per-cent. solution of cocaine. A lacerated wound or a burn soaked in a weak solution of chloretone soon becomes anesthetic, and permits of incision, suturing, etc., without pain. For other minor operations, especially about the mouth, nose, and eye, or for circumcision, it is fairly efficacious, and is used as in such weak solution as not to have any systemic effect. It is non-irritant and does not dilate the pupil, and being a very stable compound its antiseptic power may be increased by the addition of mercuric bichloride, phenol, thymol, etc.

Houghton and also Albrich have found chloretone to be readily absorbed from the stomach, and rapidly distributed throughout the body. It tends to slow the heart without weakening it, and it has no effect on the arteries or on the blood. In animals killed after large doses the greater amount of the drug is found in the brain. It is sedative and readily produces hypnosis, but has little or no effect on the important centers in the medulla oblongata. It is not

eliminated as such by the kidneys, the skin, or the lungs, and as the chlorides in the urine are increased during its administration, it is probable that the drug is broken up in the system. When chloretone is given by the mouth, the mucous membrane of the alimentary canal becomes insensitive, nausea and seasickness are relieved, and in gastric cancer or ulcer, the pain and persistent vomiting are overcome. As a hypnotic, it does not irritate the stomach or the kidneys, and has been for this purpose used in cardiac and respiratory diseases. Five to twenty grains (0.3–1.2) may be given in powder or capsule half an hour before bedtime, as its action is fairly rapid. As an anesthetic it may be used in one-per-cent. solution, either directly applied to the surface or subcutaneously. It has been used as an inhalant (1 part to 50 of liquid paraffin) in rhinitis and bronchitis. W. A. Bastedo.

Chlorides.—The chlorides used in medicine are: among the chlorides of the heavy metals, those, severally, of iron, mercury, gold and sodium, and zinc; among the chlorides of the alkalies, those, severally, of sodium, ammonium, and calcium; and among the chlorides of the alkaline earths, the chloride of barium. With the single exception of mercurous chloride (calomel), the chlorides of the heavy metals are distinguished among their sister salts for comparatively free solubility and great intensity of action. The iron, gold, and zinc chlorides are, furthermore, deliquescent to a high degree. For detailed discussion of the metallic chlorides, see articles under title of the several metals, and for barium chloride, see under *Barium*. In the case of the chlorides of the alkali bases, the influence over nutrition which they derive from their chlorine element exceeds in medicinal importance what properties are due to the basic radicle. The chlorides of the alkalies, therefore, may properly be regarded as constituting a distinct group of medicines.

Sodium Chloride.—Sodium chloride, NaCl, well known as *common salt, table salt, sea salt,* or simply *salt,* is official in the United States Pharmacopœia as *Sodii Chloridum*. It occurs as "colorless, transparent, cubical crystals, or a white, crystalline powder, odorless, and having a purely saline taste. Permanent in dry air. Soluble in 2.8 parts of water at 25°C. (77° F.), and in 2.5 parts of boiling water; almost insoluble in alcohol. When heated, the salt decrepitates; at a red heat it fuses, and at a white heat it is slowly volatilized and partly decomposed. To a non-luminous flame it imparts an intense, yellow color. An aqueous solution of the salt is neutral to litmus paper." (U. S. P.) While, as described, perfectly pure sodium chloride is permanent in the air, commercial table salt, containing, as it does, variable proportions of magnesium chloride, is more or less hygroscopic, becoming damp on exposure to moist air. Salt is the principal saline ingredient of sea water, and occurs native, also, in enormous quantities as a mineral. It is obtained for commerce from salt mines, and also, to a certain extent, by evaporating the water of the sea and of saline springs.

Sodium chloride is an important normal constituent of the body fluids, and accordingly is harmless to swallow in any ordinary quantity, if the kidneys are healthy. The only effects following its special administration are, in moderate dosage, an improvement of appetite and digestion, and probably also a quickening of assimilation and nutrition. In large single doses salt is decidedly emetic, especially if taken in a lukewarm draught, but is not sufficiently powerful for urgent requirements. Accordingly, it is used rather as an adjuvant to more active emetics, than as itself a vomiting agent. Another application of salt is its administration, dry, in quantity of a teaspoonful or so, in hemorrhage of the lungs, over which it is supposed to have some control; but such use should not be to the exclusion of more potent remedies. In the matter of external application, it is well known that salt water is more stimulating to the skin than fresh, and that, for the purpose of the constitutional reaction to be obtained, salt baths are more serviceable than fresh, and are borne by weaklings with less danger of giving "cold." The dose of salt as an appetizer is about ten grains (0.65) but the dosage is obviously very indeterminable, and much may be left to individual peculiarities of taste. As an auxiliary emetic, 240 grains (16.0), may be given in a tumblerful of lukewarm water. For saline baths sea water is best, but when not available a good substitute is afforded by a three-per-cent. aqueous solution of common table salt (a pound to four gallons). For the bathing of sensitive mucous membranes, such as the conjunctiva or the Schneiderian mucous membrane in its upper portion, a weak solution of common salt affords a fluid far less painful than simple water, for the reason that such solution approaches more nearly the normal specific gravity of the fluids of the part. The solution should range between one-half and one per cent. in strength, but it is near enough for practical purposes to make the solution by adding to a couple of fluidounces of water as much salt as will lie on the thumb nail. For injection into the nasal cavity, the solution should be blood-warm. The so-called *physiological* (commonly, though incorrectly, termed *normal*) *salt solution* is a 0.6 per cent. solution of sodium chloride in distilled water. It is largely employed for irrigation of suppurating cavities, cleansing of wounds, hypodermoclysis, enteroclysis, and in histological technique. It may be roughly prepared extemporaneously by adding a teaspoonful of sodium chloride to one pint of boiled or distilled water.

Ammonium Chloride.—This salt, NH_4Cl, commercially known as *sal ammoniac,* and still often called by the old-fashioned chemical name *muriate of ammonia,* is official in the United States Pharmacopœia only in a purified condition, under the title *Ammonii Chloridum*. Commercial sal ammoniac is now most commonly obtained from an ammoniacal liquor that occurs as a by-product in the making of illuminating gas, and is in the form of fibrous crystalline cakes of a peculiarly tough texture, making the substance very difficult to pulverize. In this condition the salt is contaminated with chloride of iron, and has to undergo a purification therefrom to fit it for medicinal use. The purified ammonium chloride presents itself as "a white, crystalline powder, without odor, having a cooling, saline taste, and permanent in the air. Soluble in 2 parts of water, in 50 parts of alcohol, and in 5 parts of glycerin at 25° C. (77° F.), and in one part of boiling water. On ignition the salt is completely volatilized, without charring." (U. S. P.)

Physiologically, ammonium chloride seems to combine to a certain extent the peculiar virtues of ammonia (see *Ammonia*) with those of the chlorides. In continuous full dosage it deranges the stomach and bowels, exciting vomiting and purging. Its medicinal applications have been very varied, but those which have best stood the test of well-observed experience are the use of the salt to relieve myalgia and some neuralgias, and to promote free expectoration in bronchial catarrhs in the second stage, especially in cases in which the secretion is thick, tenacious, and difficult to dislodge. By German practitioners the salt is much employed also in inflammatory affections, generally where there is some product of the inflammation whose reabsorption is desirable. The average dose of ammonium chloride is gr. viii. (0.5) every two or three hours. It is generally given in solution, as an ingredient of composite prescriptions, and, since its taste is very disagreeable, it is well to have a little licorice added to the mixture to disguise the flavor. *Troches of ammonium chloride* are official,

each containing 0.10 gram (gr. iss.) of the salt. Externally applied, ammonium chloride in solution is a gentle irritant, and an aqueous solution, from one to three per cent. in strength, may be used as a lotion to sluggish ulcers, etc., requiring a mildly irritant impression. A local application in respiratory catarrhs has also been devised whereby the patient inhales the salt, formed in a fine cloud in air, by an arrangement that brings together the vapors of hydrochloric acid and water of ammonia. Lastly, ammonium chloride furnishes a possible means of applying cold, since by solution in water it reduces the temperature thereof quite decidedly. Thirty-five parts each of ammonium chloride and potassium nitrate to one hundred of water will lower the temperature from ten to fifteen degrees of the Fahrenheit scale. In the absence of ice such a mixture may be put into a rubber bag and applied for purposes of refrigeration during the time that the salts are in process of dissolving.

Calcium Chloride.—Calcium chloride, $CaCl_2$, "rendered anhydrous by fusion at the lowest possible temperature," is official as *Calcii Chloridum.* Such fused salt occurs in "white, slightly translucent, hard fragments, odorless, having a sharp, saline taste, and very deliquescent. Soluble in 1.3 parts of water, and in 8 parts of alcohol at 25° C. (77° F.); in 1.5 parts of boiling alcohol, and very freely in boiling water, usually leaving a slight residue. Below a red heat the salt fuses, and, on cooling, solidifies without change in composition." (U. S. P.) Calcium chloride, because of its extreme deliquescence, must be kept in well-stoppered bottles.

Calcium chloride is credited with increasing the coagulability of the blood; and, consequently, it is administered in cases of purpura, hemophilia, aortic aneurysm and internal hemorrhages (such as hemoptysis and hematemesis). It has also been used in urticaria. In all these conditions it is advisable to give one large dose daily rather than several divided doses. Thirty grains (2.0) may be administered; and it has been claimed that doses of this size, if administered for several days beforehand, will render possible the performance of surgical operations upon hemophiliacs. Calcium chloride has a decided tonic effect on the heart and blood-vessels, and has been used to avert and to combat cardiac failure resulting from post-influenzal pneumonia. In these cases the drug should be used for a considerable period of time, in dosage of about seven grains (0.5) every four hours. Calcium lactate possesses coagulating properties similar to those of the chloride, and it is used in the same way. Dixon, however, denies this property to both of these salts when administered *per os;* but he claims that when injected under the skin, they both reduce the coagulation time of the blood very promptly.

This salt presents a combination of an acid and a basylous radicle, both of which are peculiarly effective in the determining of sound nutrition. Accordingly a course of calcium chloride has been found beneficial in cases of indurated and enlarged glands, or of a manifest scrofulous cachexia, or of tabes mesenterica. In large dose the salt is a dangerous irritant. The therapeutic dose is gr. viii. (0.5), dissolved in a wineglassful of *milk* and taken after eating.

EDWARD CURTIS.
R. J. E. SCOTT.

Chlorine.—Chlorine is a greenish-yellow gas, soluble in water, possessed of a peculiar and disagreeable odor, and an intensely irritant action upon animal tissues. Even in the comparatively weak dilution of one per cent. in air chlorine excites violent spasm of the larynx, and if actually inhaled leads to irritation and inflammation of the air passages, accompanied, perhaps, by hemorrhages, and possibly followed by death. Habit, however, establishes considerable tolerance, so that workmen in bleacheries get to breathe without distress a chlorinated atmosphere impossible of respiration to one unaccustomed. Feebly chlorinated air excites only a glow of warmth in the air passages, and an increase of bronchial mucus. Taken internally, in the form of strong chlorinated solutions, chlorine is powerfully irritant and even corrosive. In poisoning by inhalation of chlorine, the sufferer should be made to breathe cautiously the fumes of ammonia, or a weak mixture of sulphureted hydrogen in air. In poisoning by swallowing, albumin should be given freely, and the lesions treated upon general medical principles.

Chlorine has a strong affinity for hydrogen, with which body it unites to form hydrochloric acid. By virtue of this affinity chlorine can decompose water, especially in the light, appropriating the hydrogen and setting free the oxygen. Such nascent oxygen is then active for oxidizing, and will attack and decompose by oxidation any organic matter that may happen to be within reach. Vegetable coloring matters and noisome products of putrefactive or fermentative processes fall particularly easy prey to active oxygen, and as a result of their oxidation the color of the one group and the smell of the other undergo complete abrogation. In a roundabout way, therefore, chlorine, in the presence of moisture, is a powerful bleacher of organic dyes and a deodorizer of organic foulness.

Gaseous chlorine is used to deodorize, disinfect, or both. For purposes of deodorizing simply, chlorinated lime or chlorinated soda is fairly efficient, but for aërial disinfection chlorine gas must be generated in greater volume than can conveniently be gotten from those preparations. For a reasonably reliable effect, chlorine gas should be evolved in great excess of estimated minimum percentages, with the room as perfectly closed as possible, and with all articles to be disinfected as freely exposed on all sides to the atmosphere as may be. Much more commonly, however, chlorine has been used on the small scale in sick-chambers while still inhabited by the patient—a procedure which, from the point of view of genuine disinfection, is not merely futile, but leads to the positive danger of the omission of other and really potent disinfectant measures. Gaseous chlorine is most conveniently generated in considerable volume by Wiggers' method, as follows: "Mix 18 parts of finely ground common salt with 15 parts of *finely pulverized* good binoxide of manganese; put the mixture into a flask, and pour a *completely cooled* mixture of 45 parts of concentrated sulphuric acid and 21 parts of water upon it, and shake the flask; a uniform and continuous evolution of chlorine gas will soon begin, which, when slackening, may be easily increased again by *gentle* heat" (Fresenius). According to Squibb, "about two hundred grains of the common salt mixture, and half a fluidounce of the sulphuric acid mixture, liberates in the course of twelve or twenty-four hours about fifty cubic inches of chlorine, giving it off pretty rapidly for the first two or three hours, and very slowly afterward."

Locally, chlorine, applied in the form of chlorinated substances and solutions, operates as a disinfectant, detergent, and deodorant, and, by virtue of its irritant properties, also as a stimulant to healthy action in wounds and sores. The United States Pharmacopœial preparations of chlorine, available for the purposes thus suggested, are the following:

Liquor Chlori Compositus, Compound Solution of Chlorine, Chlorine Water; to replace the *Aqua Chlori* of the 1890 Edition of the Pharmacopœia. "An aqueous solution of chlorine, containing, when freshly prepared, about 0.4 per cent. of chlorine." (U. S. P.) Chlorine gas, generated by the action of diluted hydrochloric acid upon black oxide of manganese, is conducted into a bottle of distilled water until the latter, after agitation, is saturated with the gas in solution. The product, from its extreme proneness to spontaneous change, must be put up in "dark, am-

ber-colored, glass-stoppered bottles," and these completely filled and kept in a dark and cool place. Chlorine water, when freshly made, is a "clear, greenish-yellow liquid, having the suffocating odor and disagreeable taste of chlorine, and leaving no residue on evaporation. It instantly decolorizes dilute solutions of litmus, indigo, and other vegetable coloring matters." (U. S. P.) Chlorine water, especially on exposure to light, tends to lose strength by reason of the chlorine decomposing the water, and uniting with the hydrogen thereof to form hydrochloric acid; when wanted of full strength, therefore, the preparation should be freshly made.

Chlorine water is used in medicine mainly as a local application, either as a lotion for foul or indolent ulcerated surfaces upon the skin, or as a gargle in analogous conditions of the mucous membrane of the throat. If freshly made it is intolerably pungent of chlorine, and should be diluted several fold with water for use.

Calx Chlorinata.—Chlorinated Lime. This is the preparation, commonly miscalled *chloride of lime*, which results from exposing calcium hydroxide (slaked lime) to chlorine gas. The lime absorbs the chlorine with the formation of a peculiar product, which by the standard of the United States Pharmacopœia should contain "not less than thirty-five per cent. of available chlorine." Chlorinated lime is in the form of "a white, or grayish-white, granular powder, exhaling the odor of hypochlorous acid, having a repulsive, saline taste, and becoming moist and gradually decomposing on exposure to air. In water or in alcohol it is only partially soluble. The aqueous solution first colors red litmus paper blue, and then bleaches it. If chlorinated lime be dissolved in diluted acetic acid, an abundance of chlorine gas will be evolved, and only a trifling residue left undissolved." (U. S. P.) Chlorinated lime undergoes spontaneous change on exposure to air, and accordingly must be kept in well-closed vessels in a cool and dry place. If put up in glass-stoppered bottles, the stoppers must be guarded by a thin smear of paraffin, else they will become irremovably fixed to their seats.

The important chemical reaction upon which the medical virtues of the compound rest is the ready decomposition of chlorinated lime by any acid, however weak—even carbonic acid—with the evolution of free chlorine. Hence, by mere exposure to the atmosphere, the preparation continuously disengages chlorine through attack by the carbon dioxide ever present in the air, and, if treated with an acid of any power, such as hydrochloric, nitric, acetic, etc., the yield of chlorine is prompt and decided. Its only drawbacks are its chlorinous odor, its powerful bleaching action, and the fact that it attacks metals. For use as a disinfectant or deodorant, chlorinated lime may be thrown in bulk, and liberally, down privies, drains, or sinks, or into chamber vessels (of china or glass) before use; or strewn, before scrubbing, upon foul floors; or in solution, from one to three or four per cent. in water, used as a detergent lotion upon corpses, sloughing wounds, or strong-smelling feet or armpits, etc. In these various applications the preparation must not be applied strong to colored or delicate fabrics, lest the color be discharged and the texture injured. Apart from its mere deodorant property, chlorinated lime is serviceable in promoting healthy action in sluggish and foul sores, skin eruptions, etc. For this purpose a one-per-cent. lotion is a convenient form of application. A last and special application is the inhalation of the fumes of chlorinated lime in cases of poisoning by breathing sulphureted hydrogen, as may occur to workmen entering sewers. The gas is always immediately decomposed by the chlorine of the lime compound.

Liquor Sodæ Chlorinatæ.—Solution of Chlorinated Soda; Labarraque's Solution. This preparation is made by pouring a boiling-hot aqueous solution of sodium carbonate into a filtered aqueous solution of chlorinated lime. The sodium and calcium change places, calcium carbonate being precipitated, and a chlorinated compound of sodium analogous in composition to the previously existing calcium compound remaining in solution. But the sodium carbonate being ordered in excess, some of this salt, unchanged, remains in the preparation. The mixture, after filtration, is brought to standard strength by the addition of water. The product must be kept, protected from the light, in well-stoppered bottles, and if these be glass-stoppered, the stoppers should be overlaid with a thin smear of melted paraffin, else they will soon become irremovably fixed. Solution of chlorinated soda should contain "at least 2.4 per cent., by weight, of available chlorine." The preparation is "a clear, pale, greenish liquid, having a faint odor of chlorine, and a disagreeable, alkaline taste. Specific gravity about 1.050 at 25° C. (77° F.). The solution at first colors red litmus paper blue, and then bleaches it. The addition of hydrochloric acid to the solution causes an evolution of chlorine and carbonic acid gas." (U. S. P.)

Chlorinated soda has, intrinsically, properties similar to those of chlorinated lime, and, like the latter, is readily decomposed by acids with the evolution of free chlorine. Its therapeutic uses are therefore the same as those of the lime compound. The solution may be used as a deodorant disinfectant, poured down drains, sinks, or into chamber vessels of crockery or glass, or, diluted from five to tenfold, employed as a detergent and gently irritant lotion to foul ulcers, skin eruptions, etc. Like chlorinated lime, this solution has been given internally in zymotic diseases, the dose being fifteen minims (1.0), well diluted with water, and repeated every two or three hours.

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Chlorobrom is the trade name of a preparation which is said to consist of chloralamide and potassium bromide. An ounce of the mixture contains thirty grains of each of these ingredients in syrup and water. It is used as a sedative and a hypnotic; it is also a much vaunted remedy for sea-sickness. The dose is four to eight drams. R. J. E. SCOTT.

Chlorodyne.—This title has been arbitrarily applied to mixtures differing considerably in composition, none of them official in the United States Pharmacopœia. It is a valuable but dangerous remedy, and the physician should have an accurate knowledge of the amount of morphine contained in the preparation before he uses it. The dose is usually given as fifteen minims; and in this dose there may be anywhere from $\frac{1}{128}$ to $\frac{1}{4}$ grain of morphine hydrochloride. Hence, it is evident that one brand of this dangerous preparation may be thirty-two times as powerful as another brand. The National Formulary offers a "chloroform anodyne" under the title *Mistura Chloroformi et Cannabis Indicæ Composita*. N. F., Compound Mixture of Chloroform and Cannabis Indica. This preparation has a definite composition, and may be prescribed as a safe substitute for the various and variable "chlorodynes." Each fluidram of this mixture represents about seven and one-half minims of chloroform, eleven minims of tincture of cannabis indica, two minims of tincture of capsicum, and one-seventh grain of morphine sulphate; it is flavored with oil of peppermint. The average dose is thirty minims (2.0). R. J. E. SCOTT.

Chloroform.—Chloroform, chemically *trichlormethane*, $CHCl_3$ (formerly called *terchloride of formyl*, and, popularly, *chloric ether*), is an ethereal body at one time obtained by distilling cautiously a mixture of chlorinated lime, alcohol, and water, but now most commonly produced by the distillation of acetone with

chlorinated lime. Commercial chloroform is very frequently impure, and, though unobjectionable for external medical use, or, pharmaceutically, for solvent purposes, is entirely unfit for administration by inhalation as an anesthetic. Under the simple title *Chloroformum*, Chloroform, the United States Pharmacopœia recognizes a purified article "consisting of 99 to 99.4 per cent., by weight, of absolute chloroform, and 0.6 to 1 per cent. of alcohol." The presence of alcohol in purified chloroform is for preservative purposes, since absolutely pure chloroform is prone to spontaneous decomposition. Chloroform is "a heavy, clear, colorless, mobile, and diffusible liquid, of a characteristic, ethereal odor, and a burning, sweet taste. Specific gravity not below 1.476 at 25° C. (77° F.). Soluble in about 200 times its volume of cold water, and, in all proportions, in alcohol, ether, benzene, petroleum, benzin, and the fixed and volatile oils. Chloroform is volatile even at a low temperature, and boils at 60° to 61° C. (140° to 141.8° F.). It is not inflammable, but its heated vapor burns with a green flame." (U. S. P.) Chloroform is affected by light, and accordingly it should be kept in dark amber-colored bottles, which in turn should be well stoppered and stored in a cool dark place. Chloroform of standard quality is now readily obtainable, but nevertheless, since an impure article is positively dangerous for use as an anesthetic, it is well for the surgeon, before using an unknown sample, to apply the following simple tests: Pour a little of the chloroform upon a clean piece of filtering paper (or blotting paper, if filtering paper be not at hand) laid upon a clean plate or saucer. Rock the plate from side to side till the chloroform is evaporated, and as the odor of the chloroform disappears there should be no adventitious smell left to follow it. Next, shake thoroughly in a test tube a portion of the chloroform with an equal volume of distilled water, and allow the two fluids to separate by standing. The upper, aqueous portion should then not redden litmus paper, nor be affected by a five-per-cent. solution of either silver nitrate or potassium iodide.

In its action upon the animal economy, chloroform combines the properties of an irritant and a specific neurotic. It is a substance of high diffusion power, and hence capable of rapid and intense action. Applied pure to the skin in such manner as to prevent its being dissipated by evaporation, chloroform excites redness and burning pain, readily followed, if the application be prolonged, by blistering. Absorbed into the blood it produces profound perversions, of which the most important are derangement of the cerebral faculties, beginning with emotional excitement and ending in entire unconsciousness; derangement of sensation, shown most markedly in exaltation of the hearing and dulling of the tactile sense; and derangement of motility—first tremblings, or even spasms, and exaltation of reflex activity, and, later, paresis, paralysis, absolute muscular relaxation and abolition of the reflexes, and finally, if the dose be sufficient, arrest of action of heart and lungs.

For the anesthetic use of chloroform, see *Anesthesia, General Surgical.*

Elimination of absorbed chloroform is principally by the lungs and kidneys, and the greater bulk of the poison escapes unchanged.

The *therapeutic applications* of chloroform are *locally* as an addition to liniments for rubefaction, or, in dilute mixture, as an anodyne for the relief of itching or of surface pains; by the *stomach*, principally as an antispasmodic, notably in intestinal colics, where the power of chloroform is unrivalled; and by *inhalation*, as an antispasmodic, an anodyne, or, carried to full narcosis, as an anesthetic in surgical procedures.

For the *local* uses of chloroform the United States Pharmacopœia offers *Linimentum Chloroformi*, Chloroform Liniment, a preparation compounded of chloroform, three parts, and soap liniment, seven parts, by measure. In continuous application as an anodyne, this liniment should be applied under some air-proof texture to prevent the dissipation of the chloroform by evaporation. Chloroform is also much used as a local anodyne in the form of an extemporaneous ointment, made by incorporating one part of chloroform with eight or nine parts of some simple fatty basis.

For *giving by the stomach*, chloroform itself may be prescribed in extemporaneous mixture with glycerin, mucilage, or syrup. The dose ranges, for an adult, from a few drops to a teaspoonful. The latter dose, however, is a large one: it will be apt to produce decided narcotic symptoms, and often, also, vomiting. If ordered by drops, it must be remembered that the drop of chloroform is unusually small, the number required to fill the measure of 4 c.c. (fl. ℥i.) ranging from one hundred and eighty to two hundred and seventy, according to the circumstances of the dropping. Most commonly chloroform is given internally in the form of one or other of the following official preparations of the United States Pharmacopœia: *Spiritus Chloroformi*, Spirit of Chloroform. This is a solution of chloroform in alcohol of the strength of six per cent. of chloroform by measure. Dose, thirty minims (2.0), diluted in some form of mixture. *Emulsum Chloroformi*, Emulsion of Chloroform, is compounded of chloroform, expressed oil of almond, tragacanth, and water, the chloroform being present in the proportion of four parts, by measure. This emulsion keeps well, dilutes smoothly with water, and so forms a convenient preparation for the giving of chloroform. Since it contains no alcohol, the dose may be proportionately greater than that of the spirit just described, and is given in the Pharmacopœia as ℥ij (8.0). *Aqua Chloroformi*, Chloroform Water. This is simply a saturated solution of chloroform in distilled water, and is necessarily a feeble preparation, since chloroform dissolves in water but sparingly (1 part in 200). The water may be given by itself in doses of one or two tablespoonfuls, but it is more commonly used as a watery menstruum in composite prescriptions, wherein the chloroform of its composition acts as a preservative.

Toxicology.—In the matter of the toxicology of chloroform, the first point to note is that chloroform taken by swallowing, even undiluted, is much less dangerous than would be supposed. The smallest fatal dose of which the writers have read was a dram taken by a child four years old (Taylor). Witthaus says that the smallest quantity of which he can find record as having certainly caused the death of an adult, is six fluidrams (24.0). On the other hand, cases have been reported of recovery after doses of from half an ounce to four ounces. The symptoms, in poisoning by swallowing, are the production of a narcosis generally similar to that induced by inhalation of chloroform, accompanied in many cases by gastric troubles due to the direct irritation of the potion. The treatment must be conducted upon general principles, since there is no chemical antidote to the drug.

Belonging to the subject of toxicology is the question whether it is possible to narcotize a sleeping person by chloroform inhalation without the subject's first awakening from the natural slumber so as to become cognizant of the attempt. From recorded cases and the results of experiments, there seems to be no doubt but what the question is to be answered in the affirmative, *if the subject is in sound sleep* when the administration is made. But otherwise the attempt will certainly be recognized. Probably sleeping children may be more easily rendered unconscious by chloroform than adults; and children have in this way been anesthetized for surgical operations.

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END OF VOLUME II.

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